AR226-0245

HAZLETON LABORATORIES AMERICA, INC.
Chemical & BioMedical Sciences Division
3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

FINAL REPORT

SAMPLE NUMBER: 50202473

SAMPLE ENTERED: 02/15/85

REPORT PRINTED: 05/07/85

ILLAS D. ZIMMERMAN
NNESOTA MINING & MANUFACTURING COMPANY
IXICOLOGY SERVICES
. PAUL, MN 55101

MPLE: T-3727

IRCHASE ORDER NUMBER: T357842, REL. #505

ENCLOSED: ACUTE ORAL TOXICITY - METHOD, SUMMARY, PATHOLOGY
PRIMARY DERMAL IRRITATION - METHOD, SUMMARY
PRIMARY EYE IRRITATION - METHOD, SUMMARY
QAU REPORT
RAW DATA APPENDIX

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ACUTE TOXICOLOGY

BY AND FOR HAZLETON LABORATORIES AMERICA, INC.

RAW DATA FOR THIS STUDY ARE KEPT ON FILE AT HAZLETON LABORATORIES AMERICA, INC., MADISON, WISCONSIN.

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CD ORAL SCREEN

Objective: To determine the acute oral toxicity produced when a test material is administered by oral gavage to rats according to the Organisation of Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 401, Acute Oral Toxicity, adopted May 12, 1981.

Test Material: T-3727
Physical Description: Off-white waxy solid
Stability of Test Material: Sponsor has purity and stability determinations on file.

Test Animal: Young adult male and female albino rats (approximately 7 weeks of age) of the Sprague-Dawley strain were procured, maintained in group cages in temperature- and humidity-controlled quarters, provided continuous access to commercial laboratory feed and water, and held for an acclimation period of at least 7 days.

Acclimated animals were chosen at random for the study. Test animals were housed by sex in groups of five and identified by animal number and corresponding ear tag. Food and water were available ad libitum throughout the study, except for an overnight period just before test material administration when food, but not water, was withheld.

Reason for Species Selection: The rat is the animal classically used due to its small size, ready availability, and large amount of background data.

Method: Five male and five female rats weighing between 200 and 298 g were used for each dosage level. The study consisted of four dosage levels (0.20, 0.50, 2.00 and 5.00 g/kg).

Preparation and Administration of Test Material: For each dose level, the test material was mixed with corn oil and heated in a water bath to form a uniform suspension at a specified concentration. Each suspension was allowed to cool prior to dosing. An individual dose was calculated for each animal based upon its fasted body weight and was administered by gavage. The dose volume of each test mixture was 10.0 ml/kg of body weight.

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CD ORAL SCREEN (CONTINUED)

Observations: The animals were observed for clinical signs and mortality at 1, 2.5 and 4 hours following test material administration. The animals were observed daily thereafter for 14 days for clinical signs and twice daily for mortality.

All animals were weighed just before test material administration, at 7 days and at study termination. At the end of the study an acute oral LD50 was calculated for each sex.

Pathology: At study termination surviving animals were euthanatized. Animals which died during the study or were euthanatized received a gross necropsy examination and all abnormalities were recorded.

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:CD ORAL SCREEN (CONTINUED)

SUMMARY

Test Animal: Albino Rats - Sprague-Dawley strain
Source: Harlan Sprague-Dawley, Madison WI
Date Animals Received: 01/22, 02/19 and 03/19/85

Temperature and Humidity of Animal Room: 21 to 25 Degrees C.;
42 to 54% Relative Humidity

Vehicle: Corn oil
Method of Administration: Oral Gavage

Date Test Started: 03/01/85 Date Test Completed: 04/09/85

Estimated Oral LD50*: Male - 0.28 g/kg of body weight
95% Confidence Limits of 0.15 to 0.51 g/kg
Female - 0.43 g/kg of body weight
95% Confidence Limits of 0.19 to 0.97 g/kg

Mortality Summary (Number of Deaths)

Dosage Level (g/kg)	Hours 0 - 4		Days 1		2		3		4		5		6		7-14		Total		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Both
0.20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1/5	0/5	1/10
0.50	0	0	0	0	1	0	1	0	1	1	0	0	0	0	2	2	5/5	3/5	8/10
2.00	0	0	2	3	3	2	-	-	-	-	-	-	-	-	-	-	5/5	5/5	10/10
5.00	0	0	3	2	2	3	-	-	-	-	-	-	-	-	-	-	5/5	5/5	10/10

	Dosage Level (g/kg)	Average Body Weights (g) Initial	Day 7	Terminal
Male	0.20	262	277	346
	0.50	271	236	---
	2.00	254	---	---
	5.00	249	---	---
Female	0.20	225	220	240
	0.50	226	189	220
	2.00	242	---	---
	5.00	229	---	---

*Thakur, A. K., and W. L. Fazio, 1981. A computer program for estimating LD50 and its confidence limits using a modified Behrens-Reed-Muench cumulant method. Drug and Chemical Toxicology 4 (3) 297-305.

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CD ORAL SCREEN (CONTINUED)

Clinical Signs

	Hours			Days													
	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Dosage Level - 0.20 g/kg																	
Males																	
Appeared normal	5	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Diarrhea	0	0	0	2	0	0	1	1	1	0	0	0	0	0	0	0	0
Dark/red/brown-stained anal/ genital area	0	0	0	4	4	4	4	4	4	3	3	2	2	2	1	1	1
Red-stained face	0	0	0	1	4	3	3	3	3	0	0	1	1	1	0	0	0
Ocular discharge	0	0	0	0	1	2	2	2	2	0	0	0	0	0	0	0	0
Hypoactivity	0	0	0	3	3	3	4	4	4	0	0	0	0	1	0	0	0
Ataxia	0	0	0	0	0	0	2	2	2	0	0	0	0	1	0	0	0
High Carriage	0	0	0	0	0	0	0	0	0	3	1	0	0	1	0	0	0
Hypersensitivity to touch	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0
Hyperactivity	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0
Clonic convulsions	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Alopecia in abdominal region	0	0	0	0	0	0	0	0	0	4	4	4	4	4	4	4	4
Red-stained abdomen	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0	0
Piloerection	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0
Yellow-stained genital area	0	0	0	1	1	1	2	2	2	1	1	1	1	1	1	1	1
Swollen genitals	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
Prostration	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Death	0	0	0	0	0	0	0	0	0	0	0	0	0	1*	0	0	0

*Animal died in p.m.

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CD ORAL SCREEN (CONTINUED)

Clinical Signs (continued)

	Hours			Days													
	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Dosage Level - 0.20 g/kg																	
Females																	
Appeared normal	5	5	5	1	1	0	0	0	0	3	4	4	4	4	4	4	4
Diarrhea	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Hypoactivity	0	0	0	0	1	2	3	4	4	0	0	0	0	0	0	0	0
Ataxia	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
Red-stained face	0	0	0	4	4	3	3	3	3	0	0	0	0	0	0	0	0
Dark-stained anal area	0	0	0	0	2	2	2	2	2	0	0	0	0	0	0	0	0
Yellow-stained abdomen/ genital area	0	0	0	1	1	1	2	2	2	1	0	0	0	0	0	0	0
Red-stained genitals	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0	0
Alopecia in abdominal region	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
Ocular discharge	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0
Piloerection	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0

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CD ORAL SCREEN (CONTINUED)

Clinical Signs (continued)

	Hours			Days													
	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Dosage Level - 0.5 g/kg							Males										
Appeared normal	4	3	2	0	0	0	0	0	0	0	0	-	-	-	-	-	-
Diarrhea	1	2	3	4	4	3	0	0	0	0	0	-	-	-	-	-	-
Hypoactivity	0	0	0	5	4	3	2	2	2	1	0	-	-	-	-	-	-
Ataxia	0	0	0	1	2	1	0	0	0	0	0	-	-	-	-	-	-
Dyspnea	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-	-	-
Red ocular discharge	0	0	0	0	0	1	0	0	0	0	0	-	-	-	-	-	-
Red-stained face	0	0	0	4	4	3	1	1	1	0	0	-	-	-	-	-	-
Brown-stained anal area	0	0	0	4	4	3	2	2	2	1	0	-	-	-	-	-	-
Red-stained genital region	0	0	0	0	2	2	1	0	0	0	0	-	-	-	-	-	-
Hypersensitivity to touch	0	0	0	0	0	0	0	1	1	0	0	-	-	-	-	-	-
Piloerection	0	0	0	0	0	0	0	0	1	1	0	-	-	-	-	-	-
Thin appearance	0	0	0	0	0	1	0	0	0	0	0	-	-	-	-	-	-
Death	0	0	0	0	1	1	1	0	0	1	1	-	-	-	-	-	-
							Females										
Appeared normal	4	3	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Diarrhea	1	2	1	4	5	3	0	0	0	0	0	0	0	0	0	0	0
Hypoactivity	0	0	0	5	5	5	4	2	2	2	2	2	2	2	1	2	1
Ataxia	0	0	0	0	0	0	1	2	2	2	2	2	3	3	2	2	1
Convulsions	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0
Subconvulsive jerking	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Hypersensitivity to touch	0	0	0	0	0	0	0	0	0	0	0	0	2	2	1	2	1
Piloerection	0	0	0	0	0	0	0	0	0	0	0	0	2	2	1	2	1
Brown-stained anal area	0	0	0	3	4	5	4	4	4	4	4	4	4	4	3	2	2
Red-stained genital region	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
Red ocular discharge	0	0	0	0	0	1	1	1	1	1	1	1	0	0	0	0	0
Red-stained face	0	0	0	3	3	4	2	2	2	2	2	2	3	3	2	2	1
Thin appearance	0	0	0	0	0	0	0	0	0	0	0	1	3	3	2	2	1
Death	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1*	0

*Animal died in p.m.

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ICD ORAL SCREEN (CONTINUED)

Clinical Signs (continued)

	Hours			Days												
	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Dosage Level - 2.00 g/kg																	
Males																	
Appeared normal	3	2	2	0	0	-	-	-	-	-	-	-	-	-	-	-	-
Diarrhea	2	3	3	1	0	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactivity	0	0	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	0	0	0	2	0	-	-	-	-	-	-	-	-	-	-	-	-
Brown-stained anal/ genital area	0	0	0	2	0	-	-	-	-	-	-	-	-	-	-	-	-
Death	0	0	0	2	3	-	-	-	-	-	-	-	-	-	-	-	-
Females																	
Appeared normal	3	2	2	0	0	-	-	-	-	-	-	-	-	-	-	-	-
Diarrhea	2	3	3	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactivity	0	0	0	4	0	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	0	0	0	4	0	-	-	-	-	-	-	-	-	-	-	-	-
Red-stained face	0	0	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Dyspnea	0	0	0	1	0	-	-	-	-	-	-	-	-	-	-	-	-
Lacrimation	0	0	0	2	0	-	-	-	-	-	-	-	-	-	-	-	-
Yellow-stained abdomen/anal/ genital area	0	0	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Death	0	0	0	3*	2	-	-	-	-	-	-	-	-	-	-	-	-
Dosage Level - 5.00 g/kg																	
Males																	
Appeared normal	5	4	4	0	0	-	-	-	-	-	-	-	-	-	-	-	-
Diarrhea	0	1	1	2	0	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactivity	0	0	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	0	0	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Brown-stained anal region	0	0	0	2	0	-	-	-	-	-	-	-	-	-	-	-	-
Death	0	0	0	2	3	-	-	-	-	-	-	-	-	-	-	-	-
Females																	
Appeared normal	4	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-
Diarrhea	0	4	4	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactivity	1	1	1	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	0	0	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-
Dark-stained nose and mouth	0	1	2	1	0	-	-	-	-	-	-	-	-	-	-	-	-
Death	0	0	0	2	3	-	-	-	-	-	-	-	-	-	-	-	-

*Two animals died in p.m.

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CD ORAL SCREEN (CONTINUED)

PATHOLOGY

Dosage Level: 0.20 g/kg of body weight Date Dosed: 03/26/85

Animal Number	Sex	Test Day Died	Test Day Sacrificed	Necropsy Comments
C28605	M	-	14	Diffuse alopecia on ventral abdominal region.
C28574	M	-	14	No visible lesions.
C28604	M	-	14	No visible lesions.
C28547	M	11	-	Red perinasal discharge; perineum stained brown.
C28414	M	-	14	Diffuse alopecia on ventral abdominal region.
C28329	F	-	14	No visible lesions.
C28394	F	-	14	No visible lesions.
C28395	F	-	14	No visible lesions.
C28346	F	-	14	No visible lesions.
C28399	F	-	14	No visible lesions.

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CD ORAL SCREEN (CONTINUED)

PATHOLOGY (continued)

Dosage Level: 0.50 g/kg of body weight Date Dosed: 03/12/85

Animal Number	Sex	Test Day Died	Test Day Sacrificed	Necropsy Comments
C29302	M	4	-	Periocular, perinasal, and perineal areas stained dark brown; lungs - diffusely dark red.
C29313	M	2	-	Stomach - multiple, dark brown foci, up to 3 mm in length, on glandular mucosa.
C27575	M	3	-	Dark red periocular discharge (bilateral); perineum - stained dark green; stomach - glandular mucosa diffusely red, with multiple, dark green foci, pinpoint up to 1 mm in diameter, on nonglandular mucosa.
C28418	M	8	-	Stomach - raised, tan areas, up to 2 x 2 x 1 mm, on nonglandular mucosa.
C27576	M	7	-	Perineum/perianal area stained dark brown; stomach - contains dark brown material, glandular mucosa diffusely red, with multiple, raised areas, up to 1 mm in diameter, on nonglandular mucosa; small intestine - contains dark brown, mucoid material.
C28529	F	12	-	Stomach - dark brown areas, up to 1 x 5 mm, on glandular mucosa, with raised, white areas, up to 1 x 3 x 2 mm, on nonglandular mucosa.
C28534	F	-	14	No visible lesions.
C28537	F	4	-	Brown perinasal stain; stomach - dark brown foci, up to 2 mm in diameter, on glandular mucosa.
C28532	F	-	14	No visible lesions.
C28533	F	13	-	Animal thin; stomach - multiple brown areas on glandular mucosa; liver - accentuated lobular pattern on all lobes.

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ICD ORAL SCREEN (CONTINUED)

PATHOLOGY (continued)

Dosage Level: 2.00 g/kg of body weight Date Dosed: 03/06/85

Animal Number	Sex	Test Day Died	Test Day Sacrificed	Necropsy Comments
C29326	M	1	-	Stomach - contains normal food and tan granular material; small intestine - filled with tan/yellow, mucoid semifluid.
C29328	M	1	-	Stomach - contains normal food and tan granular material; small intestine - filled with tan/yellow, mucoid semifluid.
C29330	M	2	-	Stomach - glandular mucosa diffusely red; liver - accentuated lobular pattern.
C29335	M	2	-	Liver - accentuated lobular pattern.
C29331	M	2	-	No visible lesions.
C28664	F	1	-	Stomach - contains normal food and tan granular material; small intestine - filled with tan and clear, mucoid semifluid.
C28497	F	1	-	No visible lesions.
C28695	F	2	-	No visible lesions.
C28693	F	2	-	Liver - accentuated lobular pattern.
C28687	F	1	-	Liver - accentuated lobular pattern.

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CD ORAL SCREEN (CONTINUED)

PATHOLOGY

Dosage Level: 5.00 g/kg of body weight Date Dosed: 03/01/85

Animal Number	Sex	Test Day Died	Test Day Sacrificed	Necropsy Comments
C28545	M	1	-	Perineum - stained brown.
C29314	M	1	-	Perineum - stained brown.
C28198	M	1	-	Perineum - stained brown.
C29319	M	2	-	Red perinasal discharge.
C28456	M	2	-	Perineum - stained brown; red periocular discharge (bilateral); red perinasal discharge.
C28498	F	1	-	Perineum - stained brown; lungs - dark red and firm; thoracic cavity - contains a light tan granular material.
C28501	F	1	-	Perineum - stained brown.
C28500	F	2	-	Perineum - stained brown; red perinasal discharge.
C28499	F	2	-	Perineum - stained brown; red perinasal discharge.
C28503	F	2	-	Perineum - stained brown; red perinasal discharge.

Deviations from the protocol: Some rats received a commercial laboratory feed other than Purina Rodent Chow. During the study period the temperature of the animal room ranged from 21 to 25 degrees C. These deviations are not considered to have had an effect on the validity of the study.

References: Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 401, Acute Oral Toxicity, adopted May 12, 1981.

CD SKIN IRRITATION

Objective: To determine the relative level of primary skin irritation/corrosion of a test substance on rabbits under semioccluded conditions according to the Organisation of Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 404, Acute Dermal Irritation/Corrosion, adopted May 12, 1981.

Test Material: T-3727
Physical Description: Off-white waxy solid
Purity and Stability: Sponsor has purity and stability determinations on file.

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand White strain were procured, maintained individually in screen-bottom cages in temperature- and humidity-controlled quarters, provided continuous access to Teklad Laboratory Rabbit Diet and water, and held for an acclimation period of at least 7 days.

Three acclimated female animals, weighing from 2840 to 3112 g, were chosen at random for the test, treated, and maintained during the observation period as specified for the acclimation period. Test animals were identified by animal number and corresponding ear tag. Approximately twenty-four hours before treatment the hair was clipped from the back of each animal.

Reason for Species Selection: Historically, the New Zealand White albino rabbit has been the animal of choice for evaluating the effect of chemicals on the skin.

Preparation of Test Material: The sample was dosed as received.

Treatment: The test material was applied to the intact skin of each rabbit in the amount of 0.5 g per site and moistened with 0.9% saline. The treated area was covered with a 2.5 x 2.5-cm gauze patch secured with paper tape and overwrapped with Saran Wrap and Elastoplast tape to provide a semiocclusive dressing. Collars were used to restrain the test animals for the 4-hour exposure period.

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CD SKIN IRRITATION (CONTINUED)

Observations: After the exposure period, the patches were removed. The test sites were washed using lukewarm tap water and disposable paper towels. The test material was removed from the test sites as thoroughly as possible without irritating the skin. Thirty minutes following removal of the test material, the degree of erythema and edema was read according to the Draize* technique. Subsequent examinations were made at 24, 48 and 72 hours after patch removal.

Individual body weights were taken just prior to study initiation.

Pathology: At study termination all animals were euthanatized and discarded.

*Draize, J. H., "Appraisal of The Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity." Association of Food and Drug Officials of the U.S., Topeka, Kansas, pp. 46-59 (1959).

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CD SKIN IRRITATION (CONTINUED)

SUMMARY

Test Animal: Albino Rabbits - New Zealand White
Source: Hazleton Research Products, Inc., Denver PA
Date Animals Received: 02/05/85

Temperature and Humidity of Animal Room: 20 - 22 Degrees C.;
40 - 44% Relative Humidity

Date Test Started: 03/01/85 Date Test Completed: 03/04/85

Individual Dermal Irritation Scores
Test Material: T-3727

Animal Number	Erythema Score Hours 4	24	48	72	Edema Score Hours 4	24	48	72
F07819	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
F07816	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
F07800	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Primary Dermal Irritation Scores

Observation Period	3 Rabbit Mean
4 Hours:	0.0
24 Hours:	0.0
48 Hours:	0.0
72 Hours:	0.0

Results:

No dermal irritation was observed at any time during the study period.

Deviation from the protocol: The test material was moistened with 0.9% saline rather than deionized water as stated in the protocol. This deviation is not considered to have had an effect on the validity of the study.

CD SKIN IRRITATION (CONTINUED)

References:

1. Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 404, Acute Dermal Irritation/ Corrosion, adopted May 12, 1981.

2. Draize, J.H., "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics - Dermal Toxicity", Association of Food and Drug Officials of the U.S., Topeka, Kansas, pp. 46-59 (1959).

HAZLETON LABORATORIES AMERICA, INC.
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AMPLE: T-3727

ICD EYE IRRITATION

Objective: To determine the level of ocular irritation produced following a single exposure of a test substance to one eye of albino rabbits according to the Organisation for Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 405, Acute Eye Irritation/ Corrosion, adopted May 12, 1981.

Test Material: T-3727
Physical Description: Off-white waxy solid
Purity and Stability: Sponsor has purity and stability determinations on file.

Test animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand White strain were procured, maintained individually in screen-bottom cages in temperature- and humidity-controlled quarters, provided continuous access to Teklad Laboratory Rabbit Diet and water, and held for an acclimation period of at least 7 days.

Three acclimated female animals, weighing from 2666 to 3000 g, were chosen at random for the test. The animals' eyes were examined within 24 hours prior to test material administration using sodium fluorescein dye procedures. Only those animals with no sign of ocular injury or irritation were used. Test animals were identified by animal number and corresponding ear tag.

Reason for Species Selection: The New Zealand White albino rabbit is the animal of choice based upon its large orbit and nonpigmented iris.

Preparation of Test Material: The sample was dosed as received. A bulk density determination was made to determine the weight equivalent of a 0.1 ml dose. Based upon the density determination, an individual dose of 0.09 g was weighed out for each animal.

Treatment: Each rabbit received 0.09 g (0.1 ml weight equivalent) of the test material placed on the everted lower lid of one eye, with the contralateral eye serving as the untreated control. The upper and lower lids were gently held together for one second to prevent loss of material and then released. The eyes of the rabbits remained unflushed.

MPLE: T-3727

CD EYE IRRITATION (CONTINUED)

Observations: The treated eyes were observed for ocular irritation at 1, 24, 48, 72 and 96 hours after treatment. At the 72-hour reading, sodium fluorescein was used to aid in revealing possible corneal injury. Irritation was graded and scored according to the Draize* technique.

Animals were weighed just prior to test material administration.

Pathology: At study termination all animals were euthanatized and discarded.

*Draize, J.H., "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics - Dermal Toxicity." Association of Food and Drug Officials of the U.S., Topeka, Kansas, pp. 49-51 (1959).

AMPLE NUMBER: 50202473

AMPLE: T-3727

CD EYE IRRITATION (CONTINUED)

SUMMARY

Test Animal: Albino rabbits - New Zealand White
Source: Hazleton Research Products, Inc., Denver PA
Date Animals Received: 02/05/85

Temperature and Humidity of Animal Room: 19 to 22 Degrees C.;
40 to 44% Relative Humidity

Test Material: T-3727

Date Test Started: 02/28/85 Date Test Completed: 03/04/85

PRIMARY EYE IRRITATION SCORES*

OBSERVATION PERIOD	3 Rabbit Mean 0.09 g (Unwashed)
1 Hour:	7.0
24 Hours:	3.7
48 Hours:	3.0
72 Hours:	2.3
96 Hours:	0.0

* The Primary Eye Irritation Score is the total eye irritation score for all the animals divided by the number of animals (3) at each observation period.

Comments: No pain response (vocalization) was elicited from any animal following instillation of the test material.

No corneal irritation was observed during the study.

MPLE NUMBER: 50202473

MPLE: T-3727

CD EYE IRRITATION (CONTINUED)

Table 1
Individual Eye Irritation Scores

Animal Number	Observation Period	Cornea A	Cornea B	Score AXBX5	Iris A	Score A X 5	Conjunctivae A	Conjunctivae B	Conjunctivae C	Score (A+B+C)2
F07813	1 Hour	0	0	0	1	5	1	1	1	6
	24 Hours	0	0	0	1	5	1	1	0	4
	48 Hours	0	0	0	1	5	1	1	0	4
	72 Hours	0	0	0	1	5	1	0	0	2
	96 Hours	0	0	0	0	0	0	0	0	0
F07814	1 Hour	0	0	0	0	0	1	1	1	6
	24 Hours	0	0	0	0	0	1	0	0	2
	48 Hours	0	0	0	0	0	0	0	0	0
	72 Hours	0	0	0	0	0	0	0	0	0
	96 Hours	0	0	0	0	0	0	0	0	0
F07815	1 Hour	0	0	0	0	0	1	1	0	4
	24 Hours	0	0	0	0	0	0	0	0	0
	48 Hours	0	0	0	0	0	0	0	0	0
	72 Hours	0	0	0	0	0	0	0	0	0
	96 Hours	0	0	0	0	0	0	0	0	0

Table 2
Sodium Fluorescein Examination

Animal Number	Observation Period Pre-initiation	Observation Period 72 Hours
F07813	NEG	NEG
F07814	NEG	NEG
F07815	NEG	NEG

NEG = No stain retention
POS = Positive stain retention (area of cornea involved).

References:

1. Organisation for Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 405, Acute Eye Irritation/Corrosion, adopted May 12, 1981.

2. Draize J.H., "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics - Dermal Toxicity", Association of Food and Drug Official Officials of the United States, Topeka, Kansas, pp. 49-51 (1959).

QUALITY ASSURANCE STATEMENT

Study No. 50202473

The report as herein attached for the above-mentioned study has been reviewed by the assigned Quality Assurance Unit of Hazleton Laboratories America, Inc. in accordance with the Good Laboratory Practice Regulations as set forth in 21 CFR 58.35 (b) (6) (7). It has been found to accurately identify and/or describe the authorized methods and standard operating procedures followed in the conduct of the study and that the reported data accurately reflect the raw data of the laboratory study. Furthermore, the Quality Assurance Unit has conducted the following inspections of the testing facilities utilized in the conduct of this study and has submitted written reports of said inspections to the study director and/or management.

Date of Inspection	Type of Inspection	Date Issued to Management
Acute Oral Toxicity Study in Rats		
2/25-26/85	Process Audit	2/26/85
3/26/85	Process Audit	3/26/85
5/01/85	Report Review	5/01/85
Primary Dermal Irritation Study in Rabbits		
2/25-26/85	Process Audit	2/26/85
5/01/85	Report Review	5/01/85
Primary Eye Irritation Study in Rabbits		
2/25-26/85	Process Audit	2/26/85
5/01/85	Report Review	5/01/85

Diana E. Skalitzky
Inspector, Quality Assurance Unit

5/2/85
Date

ACUTE ORAL TOXICITY (LD_{50}) RECORD

Test Material T-3727 Vehicle CORN OIL RT No. 50202473

Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 3-19-85

Fasted: Date 3-25-85 Time 2:30 p.m. Tech. CK Room No. 3

♂

Sex ♂									Tech.	1985 Date	Ktron Scale Used:
Dosage 0.20 (g/kg)											
Dose Volume 10.0 (ml/kg)	Dose Time 11:55 a.m.										
Animal No./Ear Tag No. C2	8605	8574	8604	8547	8414	8576	7792		Sam	3-26	NA
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	244	250	278	279	260	258	247		Sam	3-26	KTRON 5228
Actual Dose (ml)	2.4	2.5	2.8	2.8	2.6	2.6	2.5		Sam	3-26	NA
Day 7 Body Weight (g)	254	297	324	258	252	*	*		① Sam / jp	3-26 / 4-2	15019
Day 14 Body Weight (g)	327	362	379	DEAD 4-6-85	317	*	*		jp / SP	4-9	Ktron 15019
				SP 210g		Doses Verified by			pgr	4/9	NA

① Recording error 3-26-85 Sam

♀

Dosage 0.20 (g/kg)											Ktron
Dose Volume 10.0 (ml/kg)	Dose Time 12:00 p.m.								Tech.	1985 Date	Scale Used:
Animal No./Ear Tag No. C2	8329	8394	8402	8395	8346	8381	8399		Sam	3-26	NA
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	234	218	211	200	229	215	242		Sam	3-26	KTRON 5228
Actual Dose (ml)	2.3	2.2	2.1	2.0	2.3	2.2	2.4		Sam	3-26	NA
Day 7 Body Weight (g)	284	204	*	190	204	*	249		jp	4-2	15019
Day 14 Body Weight (g)	270	218	*	209	241	*	261		jp / SP	4-9	15019
						Doses Verified by			pgr	4/9	NA

MORTALITY (NO. DIED/NO. DOSED)

Dose Level	Hours 0 - 4	Study Day 1 am	1 pm	2 am	2 pm	3 am	3 pm	4 am	4 pm	5 am	5 pm	6 am	6 pm	7 am	7 pm	8 am	8 pm	9 am	9 pm	10 am	10 pm	11 am	11 pm	12 am	12 pm	13 am	13 pm	14 am	14 pm	Total
♂ 0.20g/kg	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	0/5	0/5	0/5	0/5	0/5	0/5	NA	1/5
♀ 0.20g/kg	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	NA	0/5
Technician	Sam	Sam	Sam	CK	CK	CK	CK	Sam	Sam	Sam	Sam	CK	CK	jp	jp	SP	SP	SP	SP	CK	CK	SP	SP	SP	SP	CK	CK	SP	NA	pgr
Date	3/26	3/27	3/27	3/26	3/26	3/29	3/29	3/30	3/30	3/31	3/31	4/1	4/1	4/2	4/2	4/3	4/3	4/4	4/4	4/6	4/5	4/6	4/6	4/7	4/7	4/8	4/8	4/9	NA	4/9

NA - Not Applicable

* - Dosage calculated, but not administered
Unused animal returned to stock

Reviewed by pgr Date 4/9/85

C01121

ACUTE ORAL TOXICITY (LD_{50}) RECORD

Test Material T-3727 Vehicle CORN OIL RT No. 5D202473

Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 1-22-85

Fasted: Date 3-11-85 Time 3:00 p.m. Tech. SRM Room No. 3

Sex ♂

Dosage 0.50 (g/kg)								Tech.	1985 Date	Scale Used:
Dose Volume 10.0 (ml/kg)	Dose Time 9:25 a.m.									
Animal No./Ear Tag No. C2	9302	9313	7575	9318	7576	8418		SRM	3-12	NA
Prefasted Body Weight (g)	NA									→
Fasted Body Weight (g)	255	274	256	226	274	298		SRM	3-12	KTRON 5228
Actual Dose (ml)	2.6	2.7	2.6	2.3	2.7	① 3.0		SRM	3-12	NA
Day 7 Body Weight (g)	Dead 3-16-85	DEAD 3-14-85 SRM	DEAD 3-15-85 SP	*	Dead 3-19-85 CK	236		CK	3-19	Ktron 5228
Day 14 Body Weight (g)	185g NP	235g SRM	216g SP	*	206g CK	DEAD 3-30-85 SRM				
						Dosed Verified by Body wt. 227g		MP	3-12	NA

① writing errors 3-12-85 SRM

Sex ♀

Dosage 0.50 (g/kg)								Tech.	1985 Date	Scale Used:
Dose Volume 10.0 (ml/kg)	Dose Time 9:30 a.m.									
Animal No./Ear Tag No. C2	8529	8534	8537	8532	8531	8533		SRM	3-12	NA
Prefasted Body Weight (g)	NA									→
Fasted Body Weight (g)	231	236	223	232	211	206		SRM	3-12	KTRON 5228
Actual Dose (ml)	2.3	2.4	2.2	2.3	2.1	2.1		SRM	3-12	NA
Day 7 Body Weight (g)	160	209	Dead 3-16-85	193	*	192		CK	3-19	Ktron 5228
Day 14 Body Weight (g)	Found Dead 3-24-85 CK 160g	223	175g NP	217	*	DEAD 3-25-85 SP 184g		CK	3-26	Ktron 5228
						Dosed Verified by		MP	3-12	NA

① writing error 3-14-85 SRM

MORTALITY (NO. DIED/NO. DOSED)

Dose Level	Hours	Study Day																														Total
	0 - 4	1		① 2		3		4		5		6		7		8		9		10		11		12		13		14				
		am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm		
♂ 0.50g/kg	0/5	0/5	0/5	0/5	0/5	1/5	0/5	1/5	1/5	0/5	0/5	0/5	0/5	1/5	0/5	1/5	NA	→										→	NA	5/5	
♀ 0.50g/kg	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	0/5	2/5	1/5	0/5	NA	3/5	
Technician	SRM	SP	SP	SRM	SRM	SP	SP	MP	MP	MP	MP	CK	CK	CK	CK	SRM	SRM	CK	CK	SP	CK	CK	CK	CK	CK	SP	SP	CK	NA		pgw
Date 1985	3/12	3/13	3/13	3/14	3/14	3/15	3/15	3/16	3/16	3/17	3/17	3/19	3/16	3/19	3/19	3/20	3/20	3/21	3/21	3/22	3/22	3/23	3/23	3/24	3/24	3/25	3/25	3/26	NA	4/10	

NA - Not Applicable

* - Dosage calculated, but not administered
Unused animal returned to stock

Reviewed by pgw Date 4/10/85

GU122

ACUTE ORAL TOXICITY (LD_{50}) RECORD

Test Material T-3727 Vehicle CORN OIL RT No. 50202473

Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 1-22-85 & 2-19-85

Fasted: Date 3-5-85 Time 2:00 pm Tech. CK Room No. 3

♂

Dosage 2.00 (g/kg)										
Dose Volume 10.0 (ml/kg)	Dose Time 10:45 AM							Tech.	Date 1985	Scale Used:
Animal No./Ear Tag No. C2	9326	9330	9329	9335	9328	9327	9331	SMM	3-6	NA
Prefasted Body Weight (g)	NA									
Fasted Body Weight (g)	267	268	272	270	219	247	248	SMM	3-6	KTRON 1348
Actual Dose (ml)	2.7	2.7	2.7	2.7	2.2	2.5	2.5	SMM	3-6	NA
Day 7 Body Weight (g)	Dead 249g	DEAD 3-8-85 SP	misdosed 3-6-85 SMM	DEAD 3-8-85 SP	Dead 207	misdosed 3-6-85 SMM	DEAD 3-8-85 SP			
Day 14 Body Weight (g)	3-7-85 CBS KTron 1348	243 g		246 g	3-7-85 CBS KTron 1348		221 g			
							Doses Verified by	MP	3-6	NA

♀

Dosage 2.00 (g/kg)										
Dose Volume 10.0 (ml/kg)	Dose Time 11:00 AM							Tech.	Date 1985	Scale Used:
Animal No./Ear Tag No. C2	8663	8664	8497	8695	8692	8693	8687	SMM	3-6	NA
Prefasted Body Weight (g)	NA									
Fasted Body Weight (g)	228	251	233	253	209	247	224	SMM	3-6	KTRON 1348
Actual Dose (ml)	2.3	2.5	2.3	2.5	2.1	2.5	2.2	SMM	3-6	NA
Day 7 Body Weight (g)	*	Dead 235g	Dead 211g	DEAD 3-8-85	*	DEAD 3-8-85	Dead 211g			
Day 14 Body Weight (g)	*	3-7-85 CBS KTron 1348	3-7-85 CBS KTron 6238	SP 230g	*	SP 223g	3-7-85 CBS KTron 6238			
							Doses Verified by	MP	3-6	NA

MORTALITY (NO. DIED/NO. DOSED)

Dose Level	Hours 0 - 4	Study Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
		am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	am / pm	
♂ 2.00 g/kg	0/5	0/5 / 0/5	NA ②												→ NA	5/5
♀ 2.00 g/kg	0/5	0/5 / 0/5	NA ②												→ NA	5/5
Technician	SMM	SMM / SMM	NA												→ NA	SLH
Date 1985	3/6	3/7 / 3/7	NA												→ NA	3/11

NA - Not Applicable

* - Dosage calculated, but not administered
Unused animal returned to stock

① Entry errors 3-7-85 SMM

Reviewed by SLH Date 3-11-85

② Inadvertenly not recored mortality for study day 2 SP 3-11-85

C01123

ACUTE ORAL TOXICITY (LD_{50}) RECORD

Test Material T-3727 Vehicle Corn oil RT No. 50202473

Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 1-22-85

Fasted: Date 2-28-85 Time 5:00 pm Tech. SRM Room No. 3

Sex	Dosage 5.00 (g/kg) / Dose Volume 10.0 (ml/kg)								Dose Time 11:45 AM	Tech.	1985 Date	Scale Used:
♂	Animal No./Ear Tag No. C2	8545	8456	9314	NA	8198	9313	9319		SRM	3/1	NA
	Prefasted Body Weight (g)	NA										
	Fasted Body Weight (g)	287	264	236	266①	247	235	210		SRM	3/1	KIRON 15019
	Actual Dose (ml)	2.9	2.6	2.4	2.7	2.5	2.4	2.1		SRM	3/1	NA
	Day 7 Body Weight (g)	Dead	Dead	Dead	NA	Dead	*	Dead				
	Day 14 Body Weight (g)	Wt 278g 3-3-85 MP	Wt 244g 3-3-85 MP	Wt 227g 3-2-85 MP	↓	Wt 200g 3-3-85 MP	*	3-3-85 MP 179g		Doses Verified by	3/1	NA

① Animal not used, missing ear tag 3-1-85 SRM

③ Illegible entry, date should be 3/2/85 but not corrected or footnoted until 5-3-85 MP

Sex	Dosage 5.00 (g/kg) / Dose Volume 10.0 (ml/kg)								Dose Time 12:00 AM	Tech.	1985 Date	Scale Used:
♀	Animal No./Ear Tag No. C2	8500	8498	8497	8501	8503	8502	8499		SRM	3/1	NA
	Prefasted Body Weight (g)	NA										
	Fasted Body Weight (g)	237	231	235	230	207	223	242		SRM	3/1	KIRON 15019
	Actual Dose (ml)	2.4	2.3	2.4	2.3	2.1	2.2	2.4		SRM	3/1	NA
	Day 7 Body Weight (g)	Dead	Dead	*	Dead	Dead	*	Dead				
	Day 14 Body Weight (g)	3-3-85 MP 220g	Wt 226g 3-2-85 MP	*	Wt 217g 3-2-85 MP	3-3-85 MP 199g	*	3-3-85 MP 219g		Doses Verified by	3/1	NA

MORTALITY (NO. DIED/NO. DOSED)

Dose Level	Hours 0 - 4	Study Day 1 am	1 pm	2 am	2 pm	3 am	3 pm	4 am	4 pm	5 am	5 pm	6 am	6 pm	7 am	7 pm	8 am	8 pm	9 am	9 pm	10 am	10 pm	11 am	11 pm	12 am	12 pm	13 am	13 pm	14 am	14 pm	Total
♂ 5.00g/kg	0/5	0/5	0/5	0/5	NA																							>	NA	0/5
♀ 5.00g/kg	0/5	0/5	0/5	0/5	NA																							>	NA	0/5
Technician	SRM	MP	MP	MP	NA																							>	NA	SLH
Date 1985	3/1	3/2	3/2	3/3	NA																							>	NA	3/11

NA - Not Applicable

* - Dosage calculated, but not administered
Unused animal returned to stock

Reviewed by SLH Date 3-11-85

C01124

STUDY TITLE: Acute Oral Toxicity

RT NO. 50202473

TEST MATERIAL. T-3727

SEX ♂

DOSAGE LEVEL. 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8547

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6			
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE			
Diarrhea				✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE			
Brown stained anal area				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Red stained face					✓	NE	NE	NE	NE	NE	NE	✓	✓	✓			
ocular discharge					✓	✓	✓	✓	✓	NE	NE	NE	NE	NE			
hypoactive							✓	✓	✓	NE	NE	NE	NE	✓			
High carriage										✓	✓	NE	NE	✓			
Hyperactive										✓	✓	✓	NE	NE			
Hypersensitive to touch											✓	✓	NE	NE			
clonic Convulsion													✓	NE			
Prostration													✓	NE			
Ataxic														✓			
DEATH														①✓			
TECHNICIAN	SMM	SMM	SMM	SMM	CK	CK	SMM	SMM	CK	MO	MO	MO	CK	SP			
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6			

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

① DIED IN PM SP 4-6-85

C01125

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8604

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red Stained Face				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
diarrhea				✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Brown Stained anal/genital area				✓	✓	✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE
Alopecia Abdominal region										✓	✓	✓	✓	✓	✓	✓	✓
DEATH													②				
TECHNICIAN	Smm	Smm	Smm	Smm	CK	CK	Smm	Smm	CK	SP	CK	CK	CK SP	SP	SP	SP	SP
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

① Entry Errors SP 4-6-85

② observation done on 4/5 not recorded till 4-10-85 CK

C01126

STUDY TITLE: Acute Oral Toxicity

RT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♂

DOSAGE LEVEL: 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8605

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Hypoactive				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Red stained abdomen				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Red stained back					✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Pilo erection						✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Diarrhea							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
yellow stained genital area							✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Ataxic							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Alopecia abdominal region										~~NE~~ ✓	✓	✓	✓	✓	✓	✓	✓
High carriage										✓	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]	CK	CK	[illegible]	[illegible]	CK	[illegible]	[illegible]	[illegible]	CK	SP	SP	SP	[illegible]
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

Dentry error 4-2-85 jp

✓ - Sign Present
sl - Sign Present, Slight
NE - Not Evident
NA - Not Applicable

C01127

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8414

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Hypoactive				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Red stained genital area				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Dark stained anal area				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Red stained face					✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
ocular discharge						✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
swollen genitals							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Ataxic							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Alopecia abdominal region										✓	✓	✓	✓	✓	✓	✓	✓
High carriage										✓	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]	CK	CK	[illegible]	[illegible]	CK	[illegible]	[illegible]	[illegible]	CK	SP	SP	[illegible]	[illegible]
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

001128

STUDY TITLE: Acute Oral Toxicity

RT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♂

DOSAGE LEVEL: 0.20 g/kg

ANIMAL/KAR TAG NO. C2-8574

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Hypoactive				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Dark stained anal area				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
yellow stained genitals				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Alopecia abdominal region										✓	✓	✓	✓	✓	✓	✓	✓
DEATH																	
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]	CK	CK	[illegible]	[illegible]	CK	[illegible]	[illegible]	[illegible]	CK	SP	SP	[illegible]	[illegible]
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01429

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8395

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/24	3/24	3/24	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓
Diarrhea				✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red stained face				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Hypo active					✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
dark stained Anal area					✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
piloerection							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Ataxic								✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	Sann	Sann	Sann	Sann	CK	CK	Sann	Sann	CK	[illegible]	[illegible]	[illegible]	CK	SP	SP	SP	[illegible]
DATE 1985	3/24	3/24	3/24	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01130

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.20g/kg

ANIMAL/EAR TAG NO. C2-8394

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓
Diarrhea				✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red stained face				✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Dark stained anal Area					✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	Sma	Sma	Sma	Sma	CK	CK	Sma	Sma	CK	JD	DP	DP	CK	SP	SP	JD	JD
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01131

STUDY TITLE: Acute Oral Toxicity

RT NO. 50202473

TEST MATERIAL. T-3727

SEX ♀

DOSAGE LEVEL. 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8399

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/24	3/24	3/24	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red stained face				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Red stained genitals				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
yellow stained abdomen							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
hypoactive							✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Alopecia abdominal region										✓	✓	✓	✓	✓	✓	✓	✓
DEATH																	
TECHNICIAN	Sam	Sam	Sam	Sam	CK	CK	Sam	Sam	CK	KM	KM	KM	CK	SP	SP	SP	SP
DATE 1985	3/24	3/24	3/24	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01132

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8329

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓
Red stained face				✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
yellow stained genital area				✓	✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE
hypoactive								✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	Sam	Sam	Sam	Sam	CK	CK	Sam	Sam	CK	MP	MP	MP	CK	SP	SP	SOJ	MP
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01133

STUDY TITLE: Acute Oral Toxicity

BT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.20 g/kg

ANIMAL/EAR TAG NO. C2-8346

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9
APPEARED NORMAL	✓	✓	✓	✓	✓	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓
Hypoactive						✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
Ocular discharge						✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	Sman	Sman	Sman	Sman	CK	CK	Sman	Sman	CK	JO	MP	MP	CK	SP	SP	JOS	JO
DATE 1985	3/26	3/26	3/26	3/27	3/28	3/29	3/30	3/31	4/1	4/2	4/3	4/4	4/5	4/6	4/7	4/8	4/9

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01134

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♂

DOSAGE LEVEL: 0.5Dg/Kg

ANIMAL/EAR TAG NO.: C2-8418

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20						
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE						
Diarrhea				✓	✓	✓	NE	NE	NE	NE	NA						
Brown stained Anal Area				✓	✓	✓	✓	✓	✓	✓	NA						
Red Stained Face				✓	✓	✓	NE	NE	NE	NE	NA						
Hypoactive				✓	✓	✓	✓	✓	✓	✓	NA						
Piloerection									✓	✓	NA						
DEATH											✓						
TECHNICIAN	Sm	Sm	Sm	SP	Sm	SP	KP	KP	CK	CK	Sm						
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20						

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01135

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 0.5Dg/Kg

ANIMAL/EAR TAG NO. C2-933

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14												
APPEARED NORMAL	✓	NE	NE	NE	NE												
Diarrhea	—	✓	✓	✓	NA												
Brown Stained Anal Area	—	—	—	✓	NA												
Red stained Face	—	—	—	✓	NA												
Hypoactive	—	—	—	✓	NA												
Ataxic	—	—	—	✓	NA												
Dyspnea	—	—	—	✓	NA												
DEATH					✓												
TECHNICIAN	[illegible]	[illegible]	[illegible]	SP	[illegible]												
DATE 1985	3/12	3/12	3/12	3/13	3/14												

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01136

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♂

DOSAGE LEVEL: 0.5g/kg

ANIMAL/EAR TAG NO. C2-7576

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19							
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE							
Hypoactive				✓	✓	✓	✓	✓	✓	NA							
Red stained face					✓	✓	✓	✓	✓	NA							
Brown stained anal region					✓	✓	✓	✓	✓	NA							
Red stained genital region					✓	✓	✓	NE	NE	NA							
Diarrhea					✓	✓	NE	NE	NE	NA							
Hypersensitive to touch							---	✓	✓	NA							
DEATH										✓							
TECHNICIAN	Gram	Gram	Gram	SP	Gram	SP	DP	DP	CK	CK							
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19							

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01137

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 0.50g/kg

ANIMAL/EAR TAG NO. C2-7575

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15											
APPEARED NORMAL	✓	✓	NE	NE	NE	NE											
Diarrhea	—	—	✓	✓	✓	NA											
Brown stained anal area	—	—	—	✓	✓	NA											
Red Stained Face	—	—	—	✓	✓	NA											
Hypoactive	—	—	—	✓	✓	NA											
Ataxic	—	—	—	—	✓	NA											
DEATH						✓											
TECHNICIAN	Sam	Sam	Sam	SP	Sam	SP											
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15											

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 0.50g/kg

ANIMAL/EAR TAG NO. C2-9302

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16										
APPEARED NORMAL	NO	NE	NO	NE	NE	NE	NA										
Diarrhea	✓	✓	✓	✓	✓	✓	NA										
Brown stained anal area				✓	✓	✓	NA										
Red stained Face				✓	✓	✓	NA										
Hypoactive				✓	✓	✓	NA										
Red stained genital region					✓	✓	NA										
Ataxic					✓	✓	NA										
Appears thin						✓	NA										
Red Ocular discharge						✓	NA										
DEATH							✓										
TECHNICIAN	Sam	Sam	Sam	SP	Sam	SP	NO										
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16										

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01139

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♀

DOSAGE LEVEL: 0.5Dg/Kg

ANIMAL/EAR TAG NO. C2-8534

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/A	3/20	3/21	3/22	3/23	3/24	3/25	3/26
APPEARED NORMAL	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Diarrhea	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Brown stained Anal Area				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Red stained face				✓	✓	✓	NE	NE	NE	NE	NE	NE	✓	✓	✓	✓	✓
Hypoactive				✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Hypersensitive to touch													✓	✓	✓	✓	✓
DEATH																	
TECHNICIAN	SMM	SMM	SMM	SP	SMM	SP	MP	MP	CK	CK	SMM	CK	SP	CK	CK	SP	CK
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24	3/25	3/26

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01140

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.5Dg/Kg

ANIMAL/EAR TAG NO. C2-8529

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24		
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE		
Diarrhea				✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NA		
Brown stained Anal Area				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NA		
Red stained Face				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NA		
Hypoactive				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NA		
Ataxic							✓	✓	✓	✓	✓	✓	✓	✓	NA		
Convulsions											✓	✓	NE	NE	NA		
Hypersensitive to touch													✓	✓	NA		
Piloerection													✓	✓	NA		
Appears thin													✓	✓	NA		
DEATH															✓		
TECHNICIAN	Sam	Sam	Sam	SP	Sam	SP	CK	CK	CK	CK	Sam	CK	SP	CK	CK		
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24		

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01151

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.50g/Kg

ANIMAL/EAR TAG NO. C2-8533

STUDY DAY	HOURS 1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24	3/25	
APPEARED NORMAL	✓	NE	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Diarrhea		✓	NE	NE	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Red Stained Face				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Hypoactive				✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	✓	
Brown stained anal region					✓	✓	✓	✓	✓	✓	✓	✓	✓	NE	✓	NE	
appears thin												✓	✓	✓	✓	✓	
Piloerection													✓	✓	✓	✓	
Ataxic													✓	✓	✓	✓	
Hypersensitive to touch																✓	
DEATH																✓①	
TECHNICIAN	Sm	Sm	Sm	SP	Sm	SP	CK	CK	CK	CK	Sm	CK	SP	CK	CK	SP	
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24	3/25	

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

① entry error CK 3-23-85

② DIED IN PM SP 3-25-85

001422

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.50g/kg

ANIMAL/EAR TAG NO. C2-8532

	HOURS																
STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24	3/25	3/26
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Diarrhea				✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Brown stained Anal Area				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Hypoactive				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Red stained genital region				—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red Ocular discharge					✓	✓	✓	✓	✓	✓	✓	✓	NE	NE	NE	NE	NE
Ataxic								✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Subconvulsive Jerking								✓	NE	NE	NE	NE	NE	NE	NE	NE	NE
Appears thin													✓	✓	✓	✓	✓
Piloerection																✓	✓
DEATH																	
TECHNICIAN	Sam	Sam	Sam	SP	Sam	SP	MD	MD	CK	CK	Sam	CK	SP	CK	CK	SP	CK
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16	3/17	3/18	3/19	3/20	3/21	3/22	3/23	3/24	3/25	3/26

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

① Entry Error SP 3-15-85

C011433

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 0.5g/kg

ANIMAL/EAR TAG NO. C2-8537

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/12	3/12	3/12	3/13	3/14	3/15	3/16										
APPEARED NORMAL	✓	✓	✓	NONE		NE	NA										
Diarrhea				✓	✓	✓	NA										
Hyperactive				✓	✓	✓	NA										
Red Stained Face					✓	✓	NA										
Brown Stained anal area						✓	NA										
DEATH							✓										
TECHNICIAN	[illegible]	[illegible]	[illegible]	SP	[illegible]	SP	MP										
DATE 1985	3/12	3/12	3/12	3/13	3/14	3/15	3/16										

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

① Entry Error SP 3-15-85

C011144

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 2.00 g/kg

ANIMAL/EAR TAG NO. C2 9331

	HOURS																	
STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
SCHEDULED DATE 1985	3/6	3/6	3/6	3/7														
APPEARED NORMAL	✓	NE	NE	NE	NA													
Diarrhea		✓	✓	NE														
Hypoactive				✓														
Ataxic				✓														
Brown stained abdomen & genital area				✓														
DEATH					✓													
TECHNICIAN	Sam	Sam	Sam	JDS	SP													
DATE 1985	3/6	3/6	3/6	3/7	3/8													

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01145

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473

TEST MATERIAL. T-3727

SEX ♂

DOSAGE LEVEL. 2.0g/kg

ANIMAL/EAR TAG NO. C29330

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE 1985	3/6	3/6	3/6	3/7	3/8												
APPEARED NORMAL	NE	NE	NE	NE	NA												
Diarrhea	✓	✓	✓	NE													
Hypoactive				✓													
Ataxic				✓													
Brown stained anal area				✓	✓												
DEATH					✓												
TECHNICIAN	[illegible]	[illegible]	[illegible]	MS	SP												
DATE 1985	3/6	3/6	3/6	3/7	3/8												

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 2.0g/kg

ANIMAL/EAR TAG NO. C29326

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE ABS	3/6	3/6	3/6	3/7													
APPEARED NORMAL	✓	✓	✓	NE													
DEATH				✓													
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]													
DATE 1985	3/6	3/6	3/6	3/7													

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

001447

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 2.0g/kg

ANIMAL/EAR TAG NO. C29335

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/6	3/6	3/6	3/7	3/8												
APPEARED NORMAL	NE	NE	NE	NE	NA												
Diarrhea	✓	✓	✓	✓	↓												
Hypoactive				✓	✓												
DEATH					✓												
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]	SP												
DATE 1985	3/6	3/6	3/6	3/7	3/8												

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01448

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 2.0g/kg

ANIMAL/EAR TAG NO. C29328

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE PBS	3/6	3/6	3/6	3/7													
APPEARED NORMAL	✓	✓	✓	NE													
DEATH				✓													
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]													
DATE 1985	3/6	3/6	3/10	3/7													

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 2.0g/kg

ANIMAL/EAR TAG NO. C29687

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE 1985	3/6	3/6	3/6	3/7													
APPEARED NORMAL	NE	NE	NE	NE													
Diarrhea	✓	✓	✓	✓													
Yellow stained abdomen/genital area				✓													
Hypoactive				✓													
Ataxic				✓													
Lacrimation				✓													
DEATH				✓①													
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]													
DATE 1985	3/6	3/6	3/6	3/7													

✓ - Sign Present
sl - Sign Present, Slight
NE - Not Evident
NA - Not Applicable

①Animal died in p.m. 3-7-85 DDS

001150

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473 SEX ♀

TEST MATERIAL. T-3227 DOSAGE LEVEL. 2.0g/kg ANIMAL/EAR TAG NO. C28664...

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE 1985	3/6	3/6	3/6	3/7													
APPEARED NORMAL	✓	✓	✓	NE													
DEATH				✓													
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]													
DATE 1985	3/6	3/6	3/6	3/7													

✓ - Sign Present
sl - Sign Present, Slight

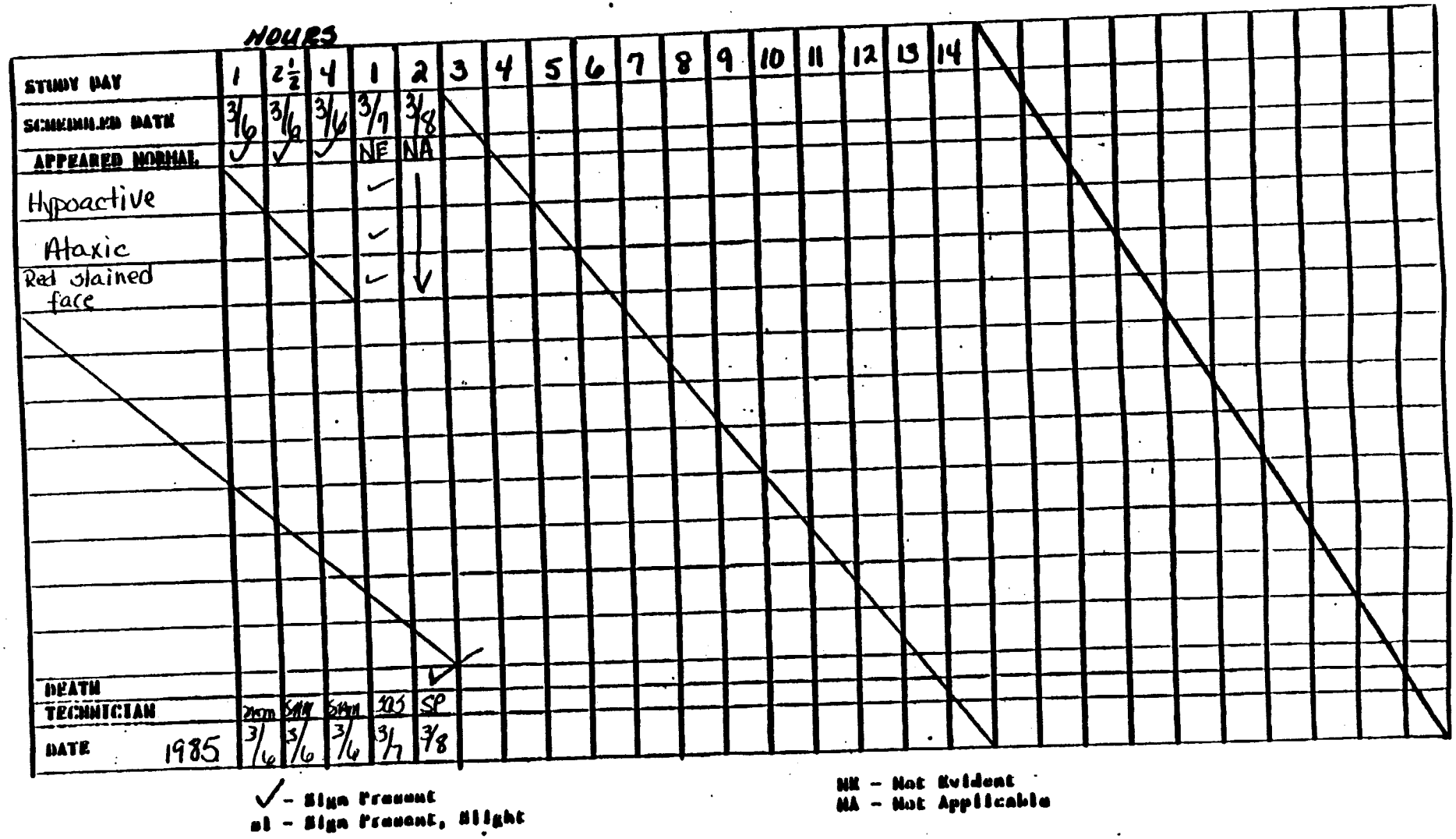
NE - Not Evident
NA - Not Applicable

001151

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473 SEX ♀

TEST MATERIAL: T-3727 DOSAGE LEVEL: 2.0g/kg ANIMAL/EAR TAG NO. C28693



✓ - Sign Present
sl - Sign Present, Slight

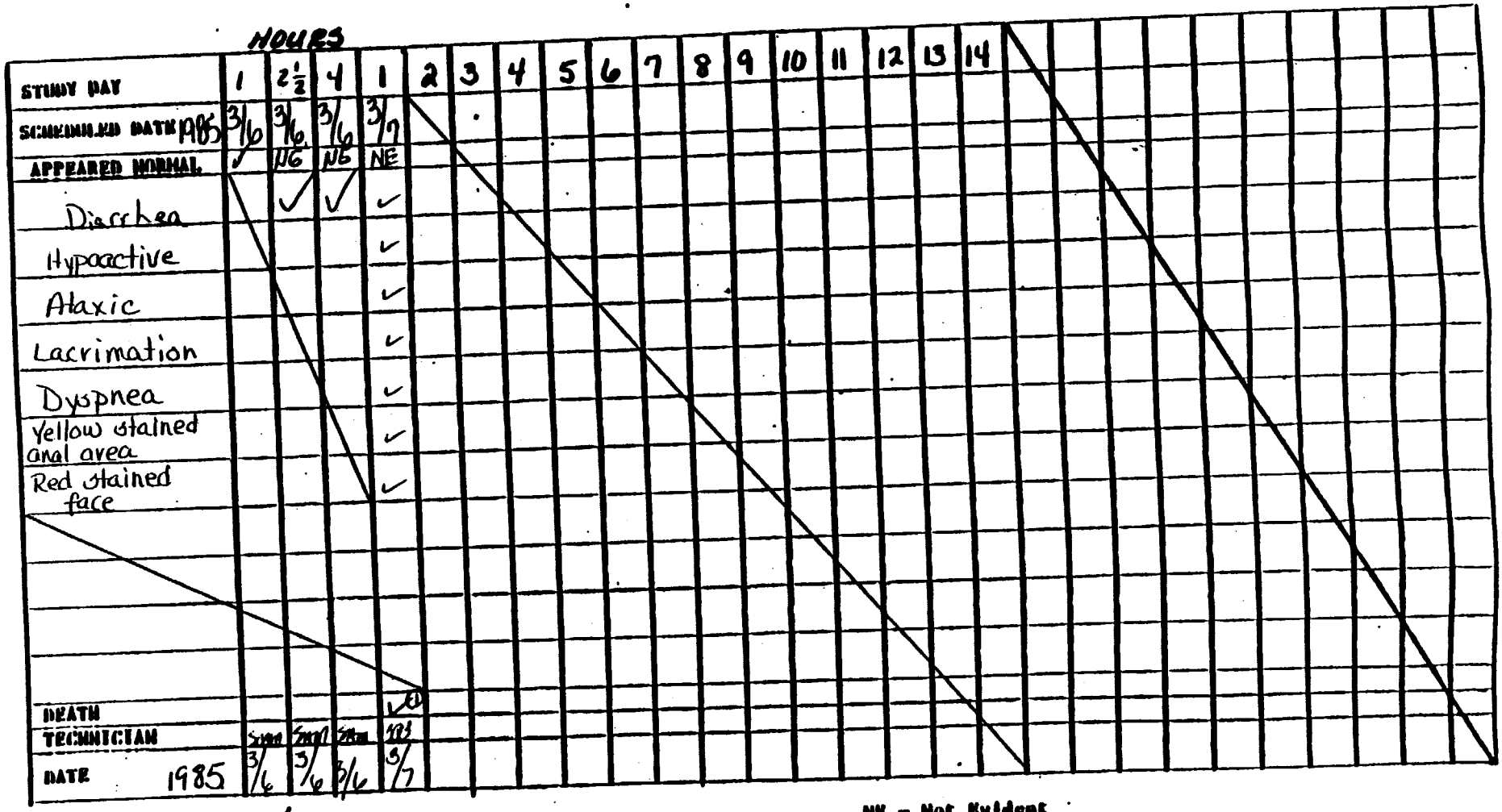
NE - Not Evident
NA - Not Applicable

C01152

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473 SEX ♀

TEST MATERIAL. T-3727 DOSAGE LEVEL. 2.00g/kg ANIMAL/EAR TAG NO. C29497



✓ - Sign Present
sl - Sign Present, Slight
NE - Not Evident
NA - Not Applicable

① Animal died in p.m. 3-7-85 CBS

C01153

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473 SEX ♀

TEST MATERIAL: T-3727 DOSAGE LEVEL: 2.0gm/kg ANIMAL/EAR TAG NO. C28695

STUDY DAY	HOURS 1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE 1985	3/6	3/6	3/6	3/7	3/8												
APPEARED NORMAL	NE	NE	NE	NE	NA												
Diarrhea	✓	✓	✓	✓													
Hypoactive				✓													
Ataxic				✓													
Yellow stained abdomen & genital area				✓													
Red stained face				✓													
DEATH					✓												
TECHNICIAN	SM	SM	SM	MB	SP												
DATE 1985	3/6	3/6	3/6	3/7	3/8												

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

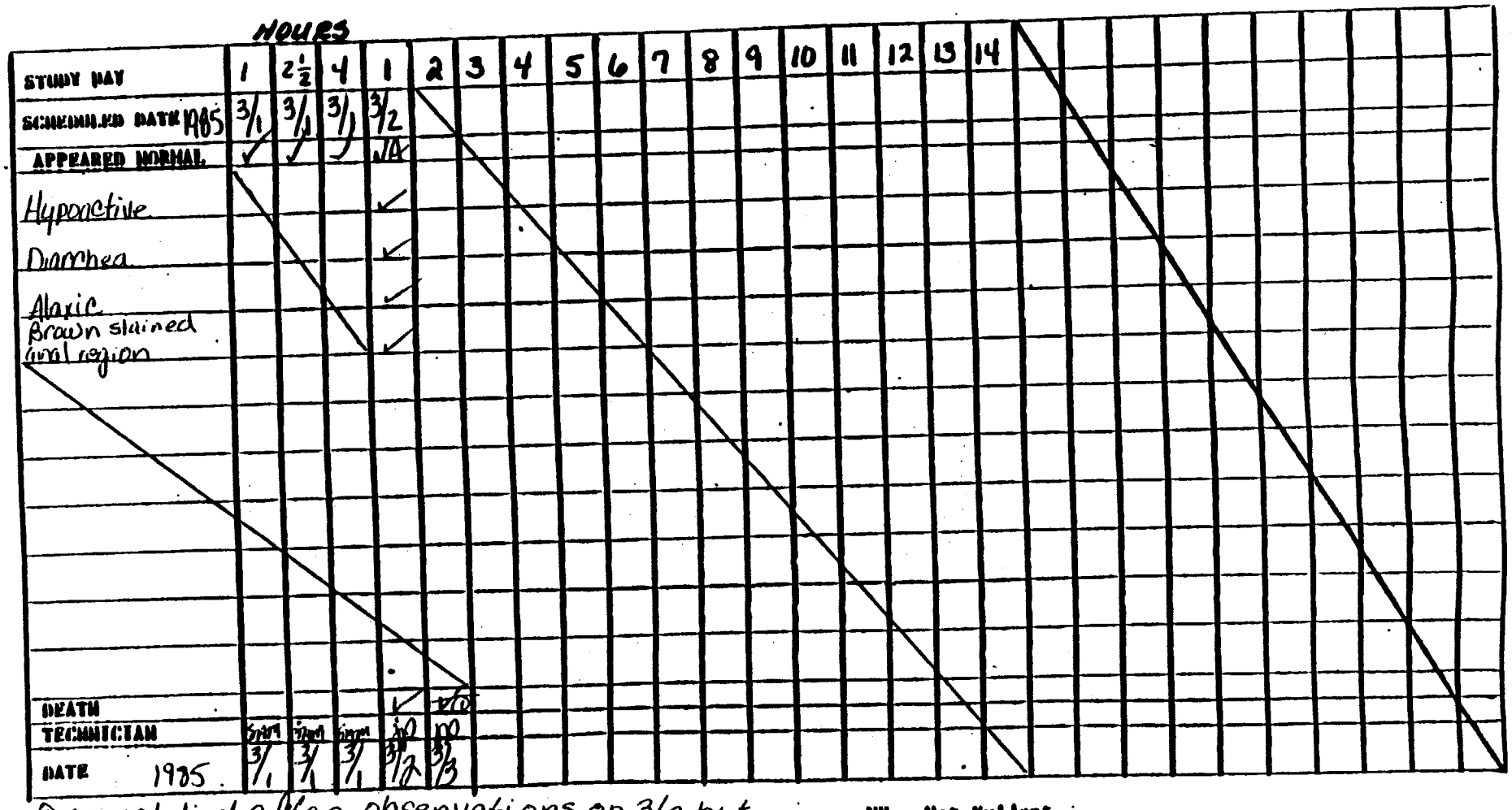
NT NO. 50202473

TEST MATERIAL: T-3727

SEX ♂

DOSAGE LEVEL: 5.00g/kg

ANIMAL/EAR TAG NO. C2-8545



① animal died after observations on 3/2 but not corrected or footnoted until 5-3-85 jp

✓ - Sign Present
I - Sign Present, Slight
NK - Not Evident
NA - Not Applicable

C01155

STUDY TITLE: Acute Oral Toxicity

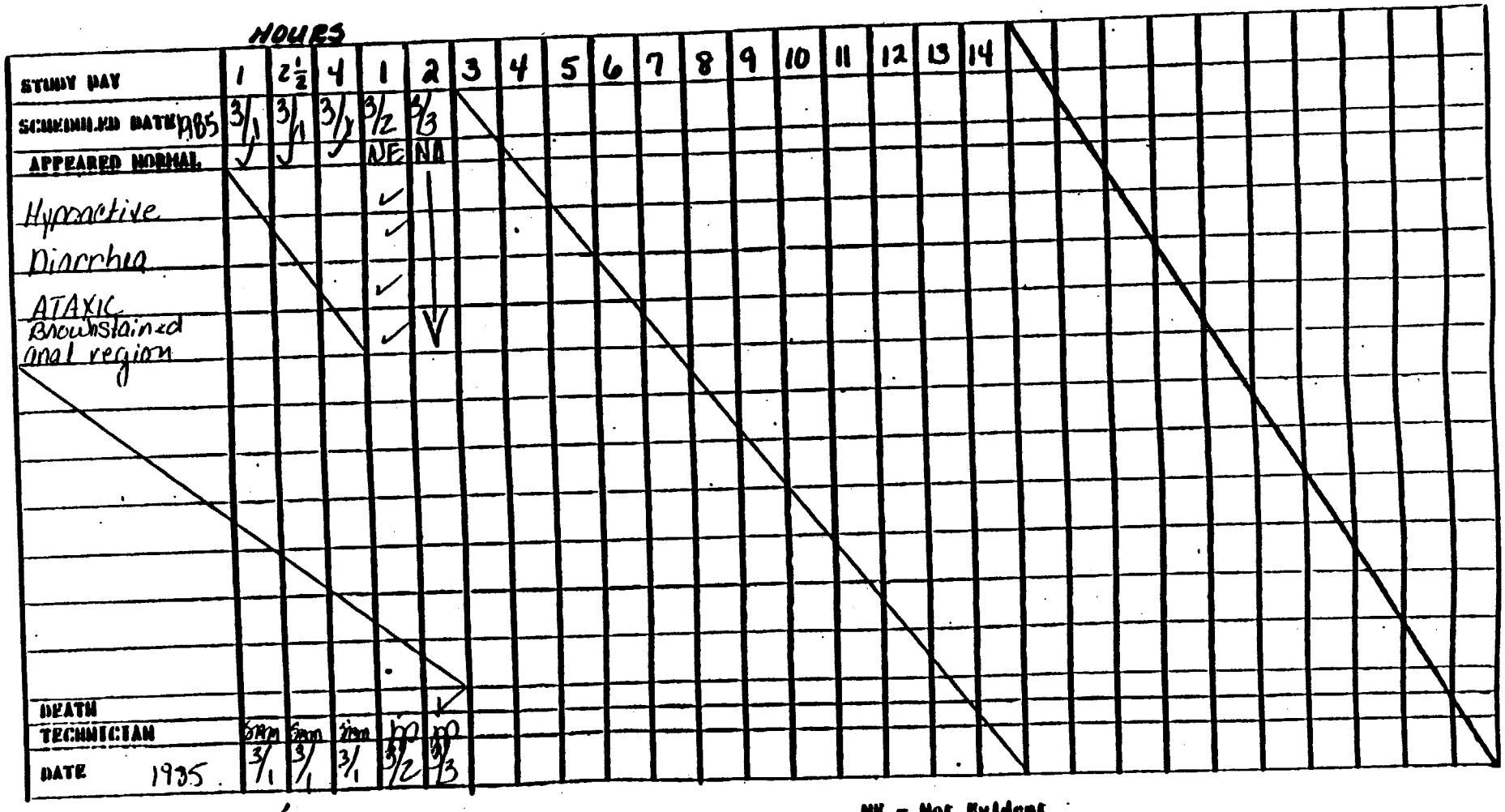
HT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♂

DOSAGE LEVEL: 5.00g/kg

ANIMAL/EAR TAG NO. C2-8456



C01156

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473

TEST MATERIAL T-3727

SEX ♂

DOSAGE LEVEL 5.00g/kg

ANIMAL/EAR TAG NO. C2-9314

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE ABS	3/1	3/1	3/1	3/2													
APPEARED NORMAL	✓	✓	✓	NA													
DEATH				↓													
TECHNICIAN	[illegible]	[illegible]	[illegible]	[illegible]													
DATE 1935	3/1	3/1	3/1	3/2													

✓ - Sign Present
sl - Sign Present, Slight

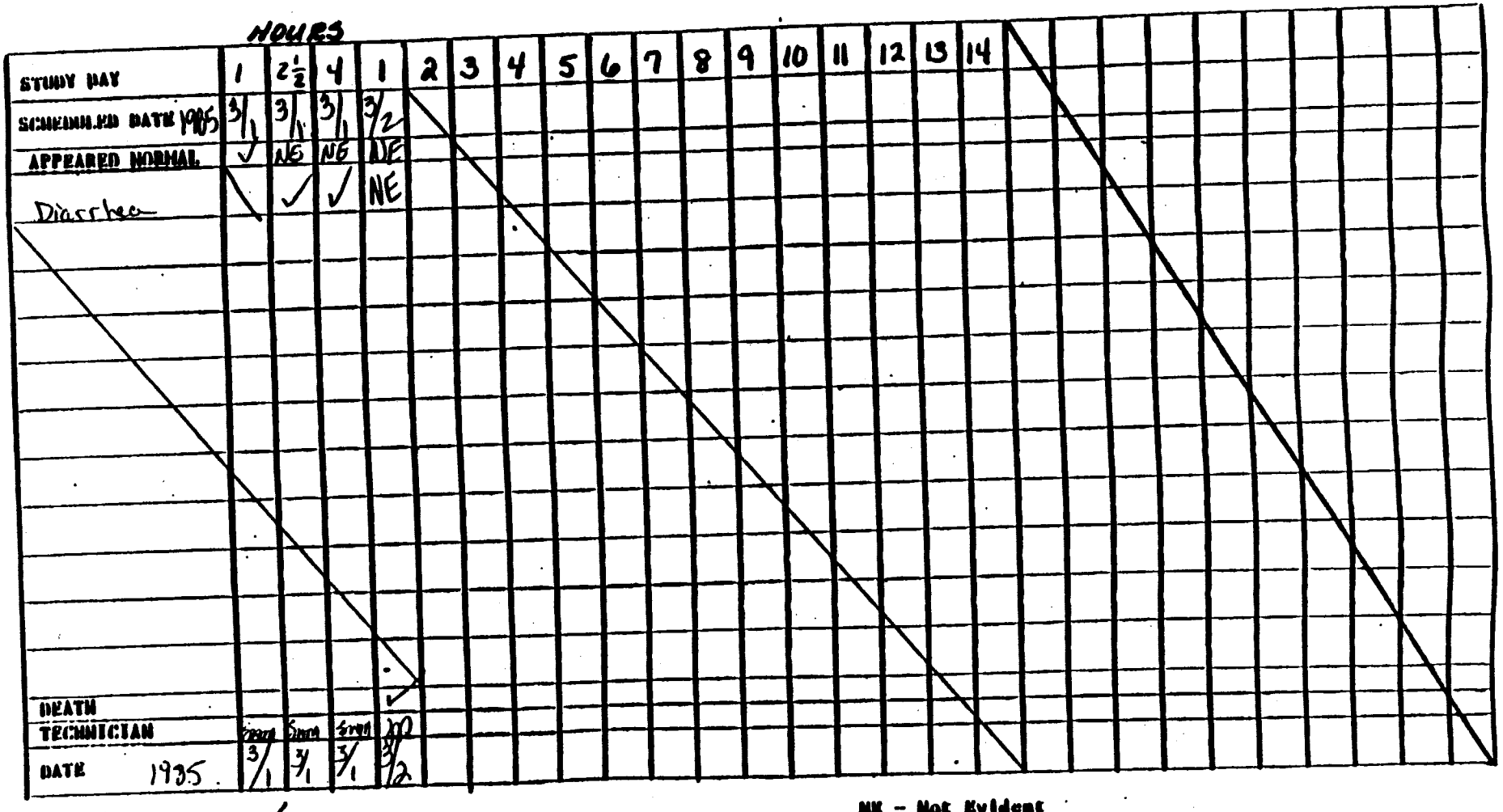
NK - Not Evident
NA - Not Applicable

C01257

STUDY TITLE: Acute Oral Toxicity

NT NO. 50202473 SEX ♂

TEST MATERIAL T-3727 DOSAGE LEVEL 5.00g/kg ANIMAL/EAR TAG NO. C2-8198



✓ - Sign Present
sl - Sign Present, Slight

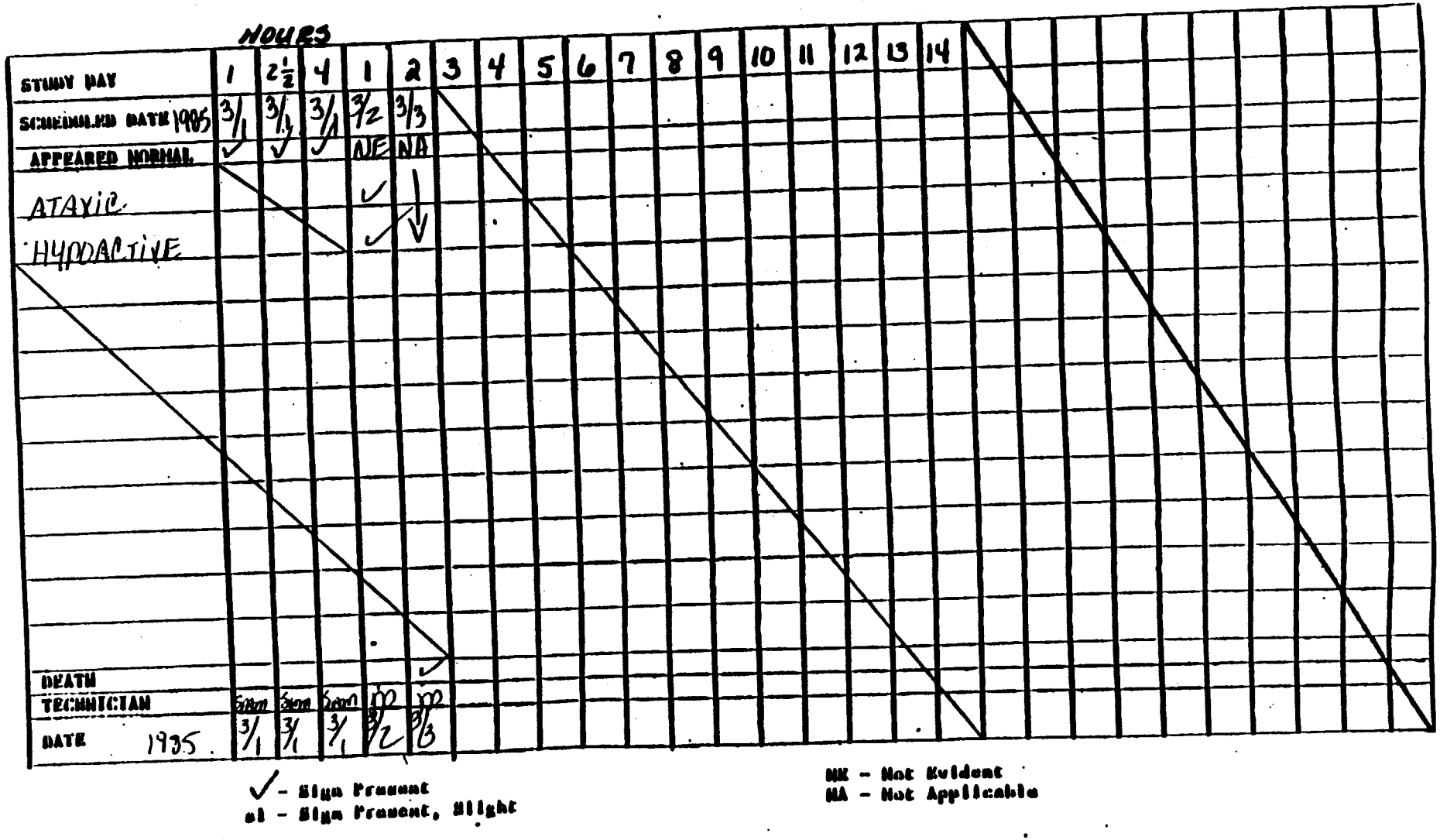
NE - Not Evident
NA - Not Applicable

C01158

STUDY TITLE: Acute Oral Toxicity

HT NO. 50202473 SEX ♂

TEST MATERIAL T-3727 DOSAGE LEVEL 5.0g/kg ANIMAL/EAR TAG NO. C2-9319



✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01159

STUDY TITLE: Acute Oral Toxicity

NT NO. 50203473

TEST MATERIAL. T-3727

SEX ♀

DOSAGE LEVEL. 5.00g/kg

ANIMAL/EAR TAG NO. C2-8498

HOURS

STUDY DAY	1	2½	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	3/1	3/1	3/1	3/2													
APPEARED NORMAL	NE	NE	NE	NA													
Hypoactive	✓	✓	✓	↓													
Dark Stained nose and mouth		✓	✓	↓													
DEATH				✓													
TECHNICIAN	am	am	am	[illegible]													
DATE 1995	3/1	3/1	3/1	3/2													

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

G01160

STUDY TITLE: Acute Oral Toxicity

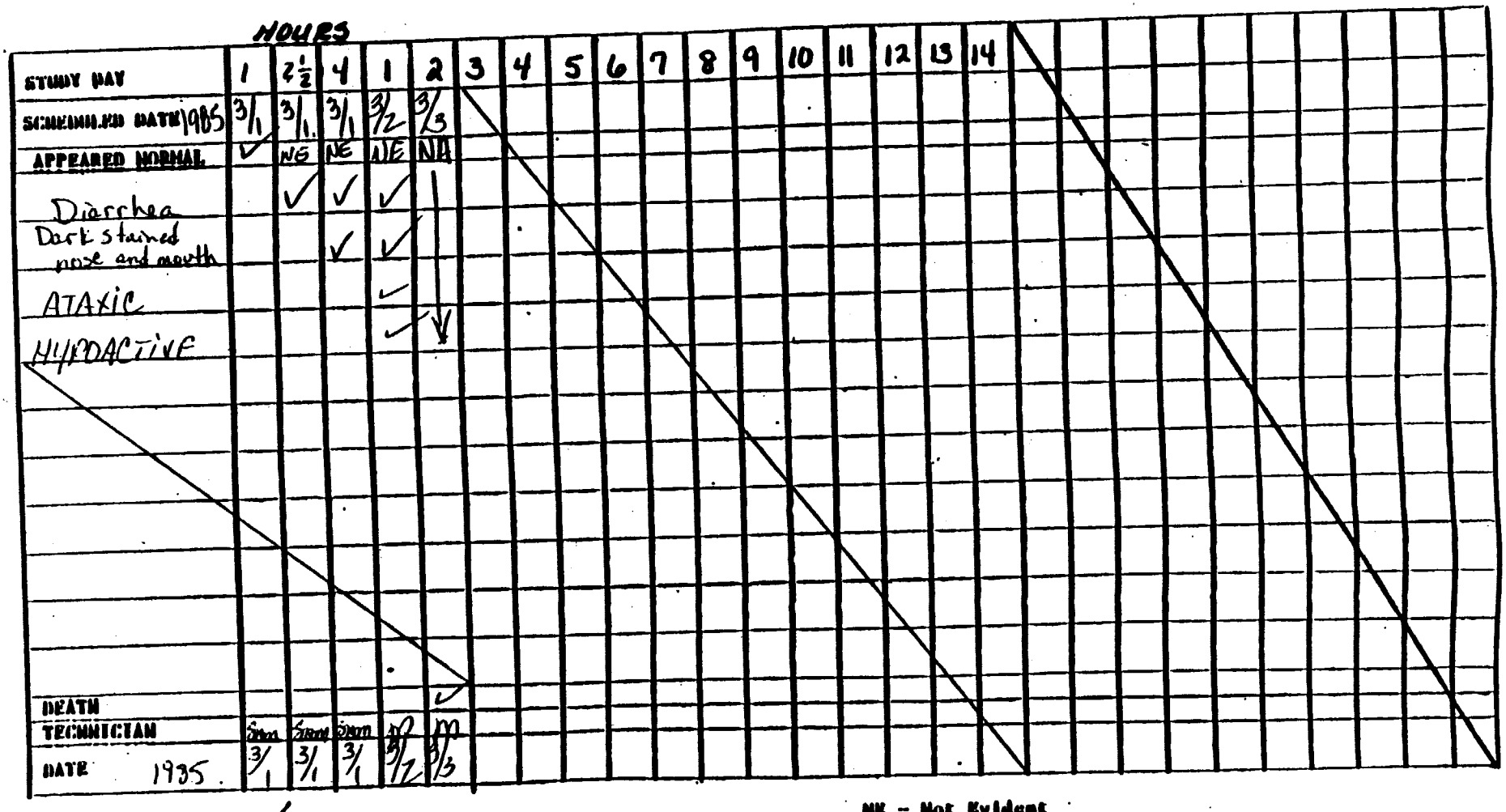
HT NO. 50202473

TEST MATERIAL: T-3727

SEX: ♀

DOSAGE LEVEL: 5.00 g/kg

ANIMAL/EAR TAG NO. C2-8499



✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01181

STUDY TITLE: Acute Oral Toxicity

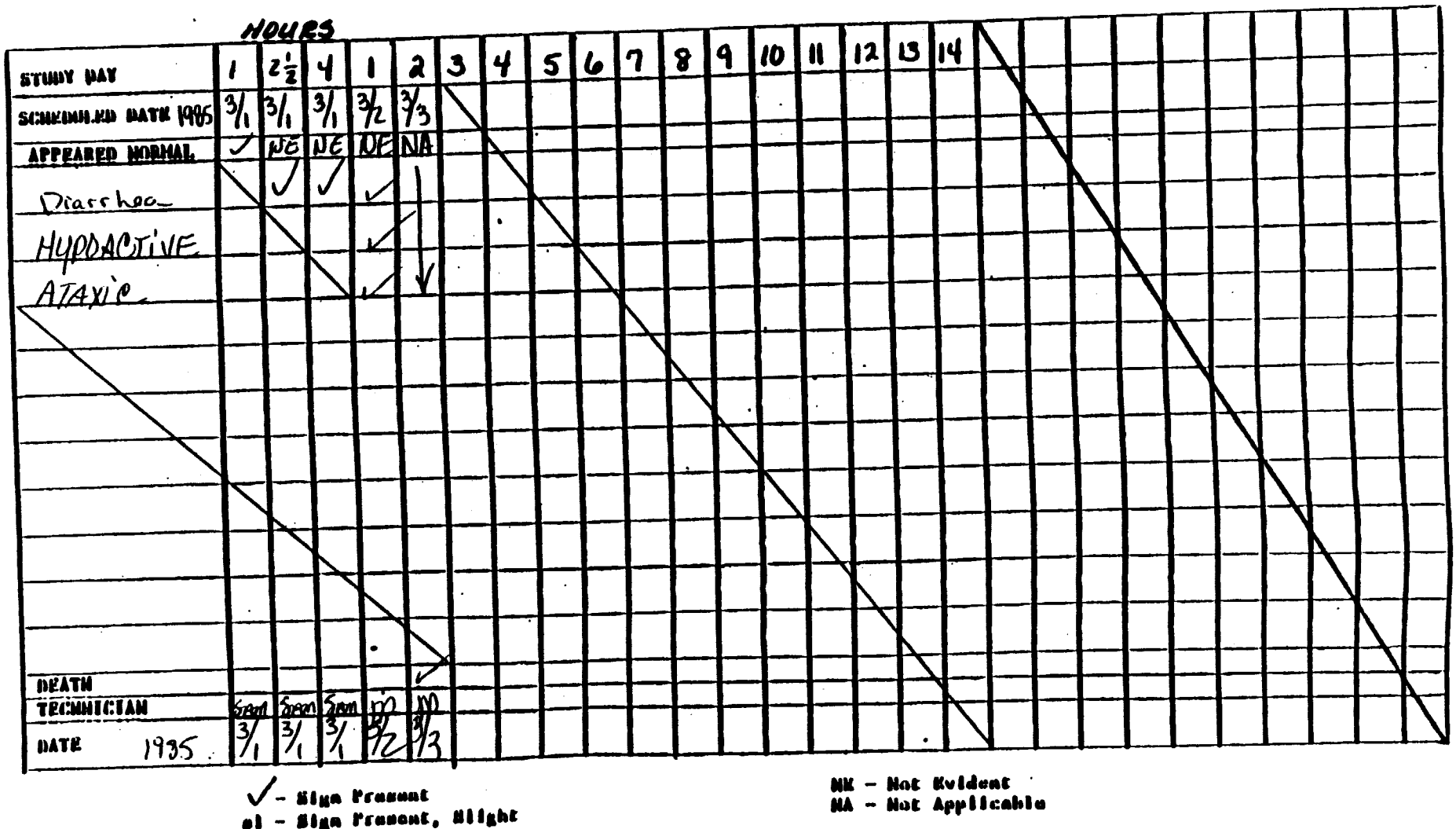
NT NO. 50202473

TEST MATERIAL. T-3727

SEX ♀

DOSAGE LEVEL. 5.00g/kg

ANIMAL/EAR TAG NO. C2-8500



✓ - Sign Present
sl - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

C01162

STUDY TITLE: Acute Oral Toxicity

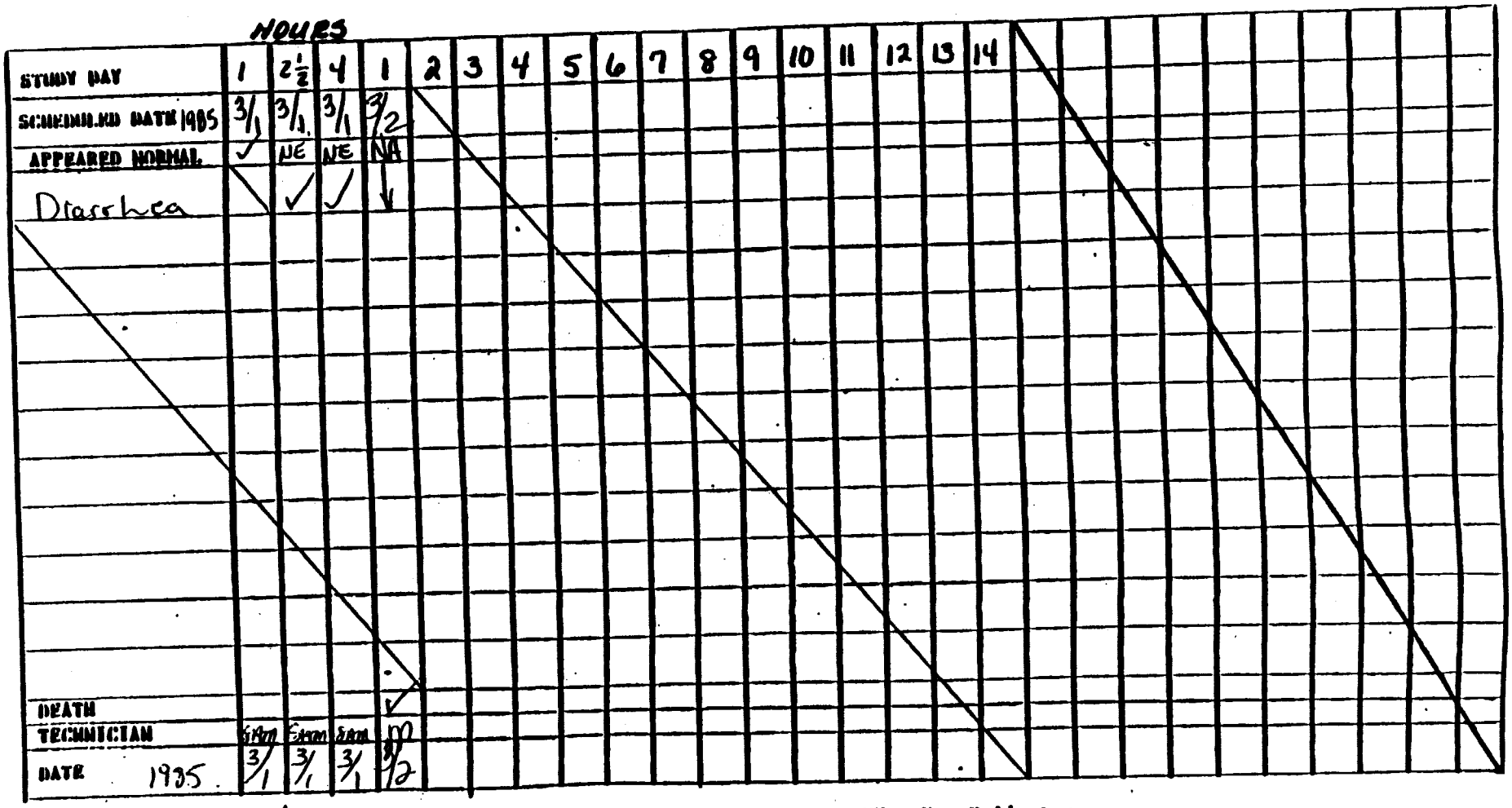
NT NO. 50202473

TEST MATERIAL. T-3727

SEX ♀

DOSAGE LEVEL. 5.00g/kg

ANIMAL/EAR TAG NO. C2-8501



✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

C01163

STUDY TITLE: Acute Oral Toxicity

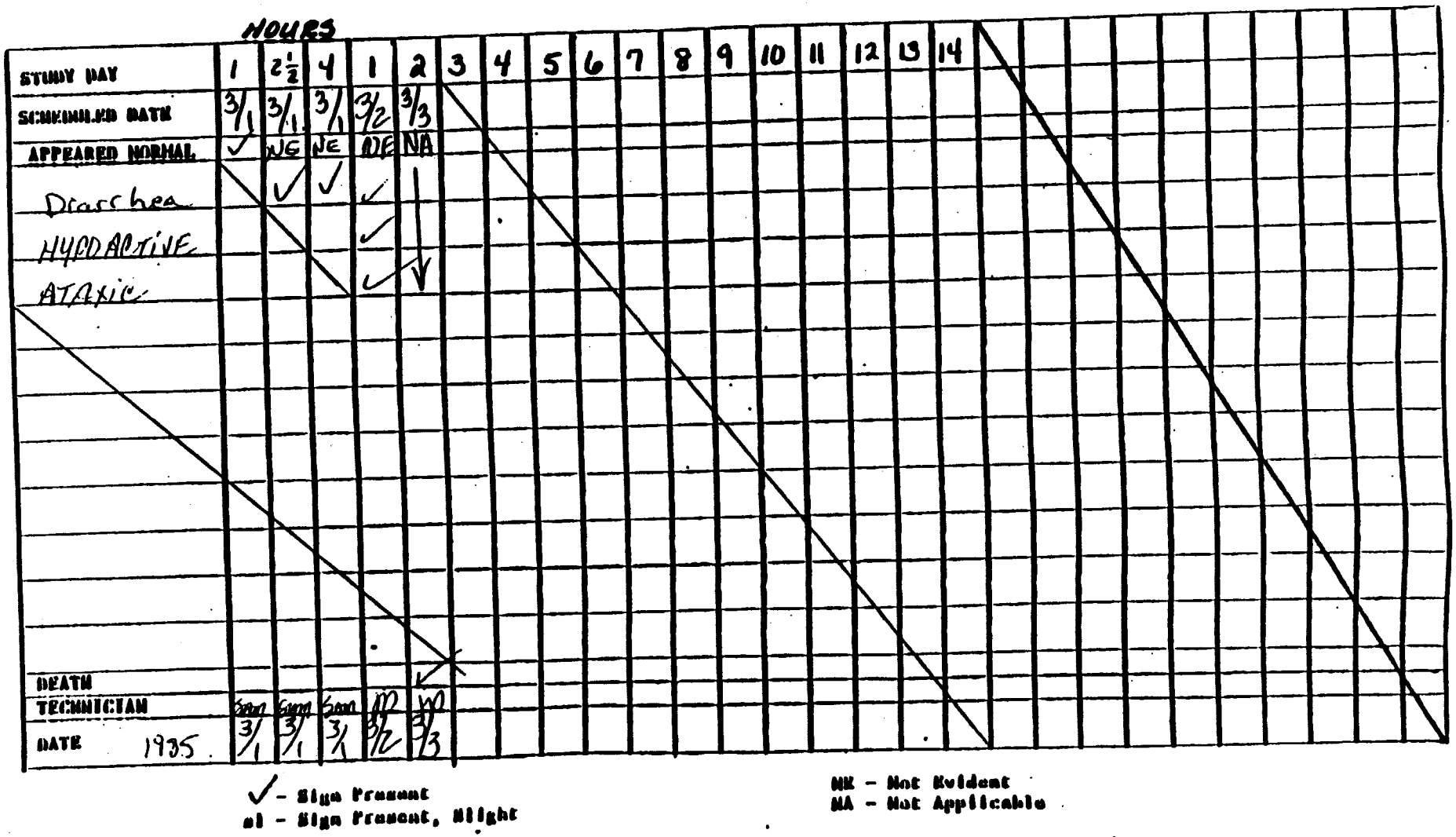
HT NO. 50202473

TEST MATERIAL T-3727

SEX ♀

DOSAGE LEVEL 5.00g/kg

ANIMAL/EAR TAG NO. C2-8503



✓ - Sign Present

sl - Sign Present, Slight

NE - Not Evident

NA - Not Applicable

PRIMARY SKIN IRRITATION SCORING SCALE

(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Highest possible erythema score	4

(2) Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Highest possible edema score	4

PRIMARY DERMAL IRRITATION STUDY

Test Compound: T-3727 30

HLA Number: 50202473

Dose: 0.5 ml/site

Vehicle: moistened with 0.9% saline

pH Result: NA

Source: Hazleton Research Products

Room Number: 161-1

Date Animals Received: 2-5-85

Date Animals Clipped: 2-28-85

Tech: CK

Initiated by: CK

Date: 3-1-85

Skin Preparation: intact

Reviewed by: MN

Date: 3-1-85

FO-		7819 ♀	7816 ♀	7800 ♀				Technician	Recorded by	1985 Date	Ktron Scale used:
Animal No./Sex								CK	CK	3-1	5921
Initial Body Weight (g)		2960	2840	3112							Dermal Irritation Score
Observation Period											
4 Hours	Erythema	0	0	0				CK	CK	3-1	0.0 SG
	Edema	0	0	0							
24 Hours	Erythema	0	0	0				MN	MN	3-2	0.0 SG
	Edema	0	0	0							
48 Hours	Erythema	0	0	0				MN	MN	3-3	0.0 SG
	Edema	0	0	0							
72 Hours	Erythema	0	0	0				CK	CK	3-4	0.0 SG
	Edema	0	0	0							
96 Hours	Erythema										
	Edema										
7 Days	Erythema										
	Edema										
7 Day Body Weight (g)											Scale used:

① Entry Error ✓ 3-1-85 CK

NA - not applicable.
A - subcutaneous hemorrhage.
B - blanching.
N - possible necrotic area.

Reviewed by: SG

Date: 3-4-85

(4251A)

C01166

PROTOCOL - APPENDIX I

(1) Cornea

(A) Opacity - degree of density (area most dense taken for reading)

No opacity	0
Scattered or diffuse area, details of iris clearly visible	1*
Easily discernible translucent areas, details of iris slightly obscured	2*
Opalescent areas, no details of iris visible, size of pupil barely discernible	3*
Opaque, iris invisible	4*

(B) Area of cornea involved

One quarter (or less), but not zero	1
Greater than one quarter, but less than half	2
Greater than half, but less than three quarters	3
Greater than three quarters, up to whole area	4

A x B x 5 Total Maximum = 80

(2) Iris

(A) Values

Normal	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive)	1*
No reaction to light, hemorrhage, gross destruction (any or all of these)	2*

A x 5 Total Maximum = 10

(3) Conjunctivae

(A) Redness (refers to palpebral conjunctivae only)

Vessels normal	0
Vessels definitely injected above normal	1
More diffuse, deeper crimson red, individual vessels not easily discernible	2*
Diffuse beefy red	3*

(B) Chemosis

No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of lids	2*
Swelling with lids about half closed	3*
Swelling with lids about half closed to completely closed	4*

(C) Discharge

No discharge	0
Any amount different from normal (does not include small amounts observed in inner canthus of normal animals)	1
Discharge with moistening of the lids and hairs just adjacent to lids	2
Discharge with moistening of the lids and hairs, and considerable area around the eye	3

Score (A + B + C) x 2 Total Maximum = 20

The total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctivae.

* Starred figures indicate positive effect.

Primary Eye Irritation Test

Initial Sodium Fluorescein Exam and Animal Body Weights

Test Compound T-3727 RT No. 50202473

pH Result NA

Dose (g) 0.09 (0.1 ml equivalent) Room No. 161-1

Dose (ml) NA Dosed By MP Date 2/28/85

Date Animals Received 2-5-85 Reviewed By pgr Date 2/28/85

Source: Hazleton Research Products

Animal No.	Sex	Initial SF*	Vocalization Following Dosing	Animal Body Weights (g) Initiation	Day 7	Day 14	Day 21
FO-7813	♀	NEG	N	2666			
7814	♀	NEG	N	2715			
7815	♀	NEG	N	3000			
TECHNICIAN	MP	(illegible)	MP	MP			
RECORDED BY	MP	(illegible)	MP	MP			
DATE	2/28 1985	2/27	2/28	2/28			
SCALE USED				KTron 5228			

* Sodium Fluorescein Examination
NEG = Negative
POS = Positive
NA = Not Applicable
Y = Yes
N = No

Time of dosing - 1:50 PM MP 2-28-85
Time of first observation - 2:50 PM MP 2-28-85

Primary Eye Irritation Test Observations

Test Compound T-3727 RT No. 50202473

Test Eye Right Group NA

NA Washed NA Seconds following instillation of test material, the test eye was washed with NA ml of NA for NA seconds ✓ Unwashed

OBSERVATION PERIOD: 1 hour

Animal No./ Ear Tag No. FO-	7813	7814	7815			
Location of Corneal Lesions Tail <——> Head	○	○	○	○	○	○
Ocular Structure						
Cornea - Opacity	0	0	0			
Area	0	0	0			
Iris	1 INJ	0	0			
Conjunctivae -						
Redness	1	1	1			
Chemosis	1	1	1			
Discharge	1 B	1 B	0			
Sodium Fluorescein Exam	NA	NA	NA			
Technician	MP	MP	MP			
Recorded By	MP	MP	MP			
Date 1985	2/28	2/28	2/28			

A = Purulent Discharge
B = Clear Discharge
C = Petite Hemorrhage
D = Blanching
INJ = Injected
NEG = Negative
POS = Positive

E = Corneal Epithelial Damage, Peeling
F = Corneal Epithelial Damage, Piling
G = Corneal Epithelial Damage, Pitting
H = Pannus
I = Corneal Neovascularization
NA = Not Applicable

Reviewed By: SG Date: 3-4-85 Eye Irritation Score: 7.0 ✓ds
(1311A)

Primary Eye Irritation Test Observations

Test Compound T-3727 RT No. 50202473

Test Eye Right Group NA

NA Washed NA Seconds following instillation of test material, the test eye was washed with NA ml of NA for NA seconds ✓ Unwashed

OBSERVATION PERIOD: 24 hours

Animal No./ Ear Tag No. FO-	7813	7814	7815			
Location of Corneal Lesions Tail <——> Head	○	○	○	○	○	○
Ocular Structure						
Cornea - Opacity	0	0	0			
Area	0	0	0			
Iris	1 INJ	0	0			
Conjunctivae -						
Redness	1	1	0			
Chemosis	1	0	0			
Discharge	0	0	0			
Sodium Fluorescein Exam	NA	NA	NA			
Technician	SAM	SAM	SAM			
Recorded By	SAM	SAM	SAM			
Date 1985	3/1	3/1	3/1			

A = Purulent Discharge
B = Clear Discharge
C = Petite Hemorrhage
D = Blanching
INJ = Injected
NEG = Negative
POS = Positive

E = Corneal Epithelial Damage, Peeling
F = Corneal Epithelial Damage, Piling
G = Corneal Epithelial Damage, Pitting
H = Pannus
I = Corneal Neovascularization
NA = Not Applicable

Reviewed By: [illegible] Date: 3-4-85 Eye Irritation Score: 3.7 14h

(1311A)

Primary Eye Irritation Test Observations

Test Compound T-3727 RT No. 50202473

Test Eye Right Group NA

NA Washed NA Seconds following instillation of test material, the test eye was washed with NA ml of NA for NA seconds ✓ Unwashed

OBSERVATION PERIOD: 48 hours

Animal No./ Ear Tag No. FO-	7813	7814	7815			
Location of Corneal Lesions Tail <——> Head	○	○	○	○	○	○
Ocular Structure						
Cornea - Opacity	0	0	0			
Area	0	0	0			
Iris	1 INJ	0	0			
Conjunctivae -						
Redness	1	0	0			
Chemosis	1	0	0			
Discharge	0	0	0			
Sodium Fluorescein Exam	NA	NA	NA			
Technician	jm	jm	~~DAP~~ jm			
Recorded By	jm	jm	jm			
Date 1985	3/2	3/2	3/2			

Delay error 3-2-85 jm

A = Purulent Discharge
B = Clear Discharge
C = Petite Hemorrhage
D = Blanching
INJ = Injected
NEG = Negative
POS = Positive

E = Corneal Epithelial Damage, Peeling
F = Corneal Epithelial Damage, Piling
G = Corneal Epithelial Damage, Pitting
H = Pannus
I = Corneal Neovascularization
NA = Not Applicable

Reviewed By: [illegible] Date: 3-4-85 Eye Irritation Score: 3 0 s/b ✓

(1311A)

Primary Eye Irritation Test Observations

Test Compound T-3727 RT No. 50202473

Test Eye Right Group NA

NA Washed NA Seconds following instillation of test material, the test eye was washed with NA ml of NA for NA seconds ✓ Unwashed

OBSERVATION PERIOD: 72 hours

Animal No./ Ear Tag No. FO-	7813	7814	7815			
Location of Corneal Lesions Tail <——> Head	○	○	○	○	○	○
Ocular Structure						
Cornea - Opacity	0	0	0			
Area	0	0	0			
Iris	1 INS	0	0			
Conjunctivae -						
Redness	1	0	0			
Chemosis	0	0	0			
Discharge	0	0	0			
Sodium Fluorescein Exam	Neg	Neg	Neg			
Technician	JM	JM	JM			
Recorded By	JM	JM	JM			
Date 1985	3/3	3/3	3/3			

A = Purulent Discharge
B = Clear Discharge
C = Petite Hemorrhage
D = Blanching
INJ = Injected
NEG = Negative
POS = Positive

E = Corneal Epithelial Damage, Peeling
F = Corneal Epithelial Damage, Piling
G = Corneal Epithelial Damage, Pitting
H = Pannus
I = Corneal Neovascularization
NA = Not Applicable

Reviewed By: SG Date: 3-4-85 Eye Irritation Score: 2.3 SG JSH

(1311A)

Primary Eye Irritation Test Observations

Test Compound T-3727 RT No. 50202473

Test Eye Right Group NA

NA Washed NA Seconds following instillation of test material, the test eye was washed with NA ml of NA for NA seconds ✓ Unwashed

OBSERVATION PERIOD: 96 hours

Animal No./ Ear Tag No. FO-	7813	7814	7815			
Location of Corneal Lesions Tail <——> Head	○	○	○	○	○	○
Ocular Structure						
Cornea - Opacity	0	0	0			
Area	0	0	0			
Iris	0	0	0			
Conjunctivae -						
Redness	0	0	0			
Chemosis	0	0	0			
Discharge	0	0	0			
Sodium Fluorescein Exam	NA	NA	NA			
Technician	CK	CK	CK			
Recorded By	CK	CK	CK			
Date 1985	3/4	3/4	3/4			

A = Purulent Discharge
B = Clear Discharge
C = Petite Hemorrhage
D = Blanching
INJ = Injected
NEG = Negative
POS = Positive

E = Corneal Epithelial Damage, Peeling
F = Corneal Epithelial Damage, Piling
G = Corneal Epithelial Damage, Pitting
H = Pannus
I = Corneal Neovascularization
NA = Not Applicable

Reviewed By: SG Date: 3-4-85 Eye Irritation Score: 0.0 SG

(1311A)

HAZLETON LABORATORIES AMERICA, INC.

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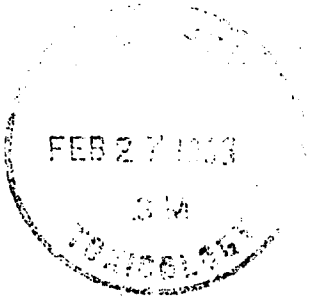
February 25, 1985



Dallas D. Zimmerman, PhD
Manager, Toxicology Services International
3M Center
St. Paul MN 55144

Dear Dallas

Enclosed please find two copies each of the following protocols for sample T-3727, HLA No. 50202473:

Protocol No.	Study
TP-2069	Acute Oral Toxicity Study in Rats
TP-2072	Primary Eye Irritation Study in Rabbits
Tp-2071	Primary Dermal Irritation Study in Rabbits

These studies will be conducted in accordance with the OECD testing guidelines and GLP regulations.

Please sign all copies, retain one set for your file, and return the others to me. We can initiate these studies upon your verbal authorization.

Should you have any questions, please feel free to call.

Sincerely

Steven M. Glaza
Study Director
Acute Toxicology

SMG/mvh
Enclosures

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PROTOCOL TP2071

Primary Dermal Irritation Study in Rabbits (OECD Guidelines)

Study No. 50202473

for

3M
St. Paul, Minnesota

by

Hazleton Laboratories America, Inc.
Life Sciences Division
3301 Kinsman Boulevard
Madison, Wisconsin 53704

February 25, 1985

PROTOCOL TP2071

Primary Dermal Irritation Study in Rabbits
(OECD Guidelines)

Study No.	50202473
Study Location	Hazleton Laboratories America, Inc. Life Sciences Division 3301 Kinsman Boulevard Madison, Wisconsin 53704
Test Material	T-3727
Sponsor's Representative	Dallas D. Zimmerman, PhD
Study Director	Steven M. Glaza
Proposed Timetable	
Starting Date	Week of February 25, 1985
Completion Date	Week of February 25, 1985
Final Report Date	Week of April 1, 1985

OBJECTIVE

The objective of this study is to determine the relative level of primary skin irritation of a test material on rabbits under semioccluded conditions. All aspects of this study will conform to the Organisation for Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 404, Acute Dermal Irritation/Corrosion, Adopted May 12, 1981[1] and the U.S. Food and Drug Administration's Good Laboratory Practice Regulations for Nonclinical Laboratory Studies.[2] All procedures will be done according to Hazleton Laboratories America, Inc. (HLA) Standard Operating Procedures (SOPs) referenced in this protocol.

TEST MATERIAL

Test Material:	T-3727.
Physical Description:	Off-white solid.
Purity and Stability:	Sponsor has purity and stability determinations on file.
Storage Conditions:	Store at room temperature.
Test Material Retention:	Any unused test material will be discarded 30 days after issuance of the final report.
Safety Precautions:	Laboratory personnel will take the normal necessary precautions in handling a substance of unknown toxicity. Laboratory clothing, latex gloves, safety glasses, and a particle mask approved for toxic dusts must be worn.

TEST SYSTEM

Test Animal

Young adult albino rabbits of either sex of the New Zealand White strain, approximately 14 weeks of age, will be obtained from Hazleton Research

Products Inc., Denver, Pennsylvania. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. Historically, the New Zealand White albino rabbit has been the animal of choice for evaluating the effect of chemicals on the skin.

Acclimation

Upon receipt, the animals will be taken to a designated animal room where they will be acclimated for at least 1 week before being placed on test (OP-GENB 36). During acclimation, the animals will be examined for clinical abnormalities indicative of health problems (e.g., diarrhea, ectoparasites, rough hair coat, nasal or ocular discharge, evidence of injury, etc.). Any animals regarded as unsuitable for study purposes because of poor physical condition will not be released from acclimation and the reason(s) will be documented.

Identification

Each animal in the study will be assigned a permanent identification number and will be identified with a metal ear tag (OP-GENB 24). All data collected from an animal will be recorded and filed under its identification number.

Housing and Maintenance

The following environmental conditions will be maintained in the animal room used for this study (OP-TARC 230).

- Temperature: 21°C ±2°
- Relative humidity: 50% ±20%
- Air change: At least 10 changes an hour of filtered 100% outside air
- Light cycle: 12 hours light/12 hours dark

Temperature and humidity will be monitored throughout the study. Variations from prescribed environmental conditions will be documented.

Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals."[3] Care will be taken to ensure that the animals are not disturbed for reasons other than data collection and routine maintenance. The animals will be housed individually in screen-bottom stainless steel cages (heavy gauge) held on racks, with absorbent pan liners in the urine- and feces-collecting pans. Pan liners will be changed at least three times each week.

Feed and water will be provided ad libitum. The diet will be Teklad Laboratory Rabbit Diet. No contaminants are expected to be present in the feed or water which would interfere and affect the results of the study.

Study Design

Three rabbits will be selected at random based upon health and a body weight of 2.0-3.5 kg. Each animal will serve as its own control.

PROCEDURES

Preparation and Administration of Test Material

Twenty-four hours prior to test material administration, the hair will be clipped from the back and flanks of each animal. The treatment sites will be inspected for interfering lesions, irritation, or defects that would preclude the use of any of the animals.

The test material will be applied to the test area (approximately 6 cm^2) on each rabbit, in the amount of 0.5 g and will be moistened with deionized water. The treated area will be covered with a 2.5-cm x 2.5-cm gauze patch

secured with paper tape and loosely overwrapped with Saran Wrap and Elastoplast tape to provide a semiocclusive dressing. Collars will be used to restrain the animals during the 4-hour exposure period.

Reason for Route of Administration

Historically, the route of choice based on the method of Draize.[4]

Observations

After the 4 hours of exposure the patches and the test material will be removed as thoroughly as possible using water or an appropriate solvent without irritating the skin. Thirty minutes after removing the patches, the degree of erythema and edema will be recorded according to the Draize Technique (Attachment 1). Subsequent readings will be taken at 24, 48, and 72 hours after patch removal. Further observations may be recorded, as necessary, to establish reversibility. If irritation is increasing in severity at the 72-hour examination period, observations will be repeated at 96 hours and at 7 and 14 days, if applicable.

Body weights will be taken just prior to test material administration and at weekly intervals during the study. Observations and body weights will be recorded in the study notebook.

Pathology

All animals, whether dying on test or sacrificed at study termination, will be discarded.

Report

The final report will present a description of the test material, a description of the test system, dates of study initiation and termination, a tabulation of irritation data, and a description of any toxic effects other than dermal irritation.

Maintenance of Raw Data and Records

Original data or copies thereof will be available at HLA to facilitate auditing the study during its progress and prior to acceptance of the final report. When the final report is completed, all original paper data, as well as the final report, will be retained in the archives of HLA, Madison, Wisconsin (OP-GEN 44).

REFERENCES

1. "Acute Dermal Irritation/Corrosion", OECD Guidelines for Testing Chemicals, Section 404, May 12, 1981.

2. 21 CFR 58

3. DHEW Publications No. (NIH) 78-23 (1978).

4. Draize, J. H., "Dermal Toxicity," Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Association of Food and Drug Officials of the U.S., Topeka, Kansas, pp. 46-59 (1959).

PROTOCOL APPROVAL

Dallas D. Zimmerman — 2-25-85

Dallas D. Zimmerman, PhD
Sponsor's Representative
3M

Date

Steven M. Glaza — 2-25-85

Steven M. Glaza
Study Director
Group Leader, Acute Toxicology
Hazleton Laboratories America, Inc.

Date

(1069S/jg)

ATTACHMENT I

PRIMARY SKIN IRRITATION SCORING SCALE

1. Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Highest possible erythema score	4

2. Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Highest possible edema score	4

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PROTOCOL TP2069

Acute Oral Toxicity Study in Rats (OECD Guidelines)

Study No. 50202473

for

3M
St. Paul, Minnesota

by

Hazleton Laboratories America, Inc.
Life Sciences Division
3301 Kinsman Boulevard
Madison, Wisconsin 53704

February 25, 1985

PROTOCOL TP2069

Acute Oral Toxicity Study in Rats
(OECD Guidelines)

Study No.:	50202473
Study Location:	Hazleton Laboratories America, Inc. Life Sciences Division 3301 Kinsman Boulevard Madison, Wisconsin 53704
Test Material:	T-3727
Sponsor's Representative:	Dallas D. Zimmerman, PhD
Study Director:	Steven M. Glaza
Proposed Timetable	
Starting Date:	Week of February 25, 1985
Completion Date:	Week of March 11, 1985
Final Report Date:	Week of April 1, 1985

OBJECTIVES

To determine the acute oral toxicity produced when the test material is administered by the oral route (gavage) to rats. All aspects of this study will conform to the Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 401, adopted May 12, 1981[1] and the U.S. Food and Drug Administration's Good Laboratory Practice Regulations for Nonclinical Laboratory Studies.[2] All procedures will be done according to Hazleton Laboratories America, Inc. (HLA) Standard Operating Procedures (SOPs) referenced in this protocol.

TEST MATERIAL

Test Material:	T-3727.
Physical Description:	Off-white solid.
Purity and Stability:	Sponsor has purity and stability determinations on file.
Storage Conditions:	Store at room temperature.
Test Material Retention:	Any unused test material will be discarded 30 days of issuance of the final report.
Safety Precautions:	Laboratory personnel will take the normal necessary precautions in handling a substance of unknown toxicity. Laboratory clothing, latex gloves, safety glasses, and a particle mask approved for toxic dusts must be worn.

Disposal

All waste feed, animal wastes, pan liners, and carcasses resulting from this study will be disposed of in a high-temperature incinerator (U.S. Smelting Furnace Company, Belleville, Illinois).

TEST SYSTEM

Animal Model

Young adult male and female albino rats (approximately 7 weeks of age) of the Sprague-Dawley strain will be obtained from Harlan Sprague-Dawley, Madison, Wisconsin. Rats will be selected at random from healthy animals that had been acclimated at HLA for at least 1 week. An adequate number of extras will be purchased in order that no animal in obviously poor health is placed on test. The weight variation in animals used on test will not exceed ±20% of the mean weight (i.e., mean = 250 g, range = 200 to 300 g).

Reason for Species Selection

The rat is the animal classically used due to its small size, ready availability, and large amount of background data.

Identification

Each animal will be assigned an individual animal number and ear tag which will accompany data collected from that animal throughout the study (OP-GENB 24).

Housing and Maintenance

The following environmental conditions will be maintained in the animal room used for this study (OP-TARC 230).

- Temperature: 22°C ±2°
- Relative humidity: 50% ±20%
- Air change: At least 10 changes an hour of filtered 100% outside air
- Light cycle: 12 hours light/12 hours dark

Temperature and humidity will be monitored throughout the study. Variations from prescribed environmental conditions will be documented.

Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals."[3] Care will be taken to ensure that the animals are not disturbed for reasons other than data collection and routine maintenance. The animals will be individually housed in screen-bottom stainless steel cages held on racks, with absorbent pan liners in the urine- and feces-collecting pans. Pan liners will be changed at least three times each week.

Feed and water will be provided ad libitum. The diet will be Purina Rat Chow®. No contaminants are expected to be present in the feed or water which would interfere and affect the results of the study.

PROCEDURES

Experimental Design

Initially, a single dose of 5.0 g/kg will be administered to 10 animals (five males and five females). If no test material-related mortality is produced at this level, no further testing is required. If any mortality occurs at the 5.0-g/kg dose level, at the Sponsor's request, three or four geometrically spaced dose levels may be added. Each dose level will consist of 10 animals (five males and five females). Animals will be assigned to groups according to HLA Standard Operating Procedure OP-TOX 42.

Test Material Preparation and Administration

The test material will be suspended in an appropriate vehicle. Individual dosages will be calculated based upon the animal's body weight taken just before administration of the test material and administered by gavage.

Justification of Route of Administration

This is the method for administering a known quantity of test substance and has been the route of choice historically.

Observations

The animals will be observed individually for clinical signs and mortality at 1.0, 2.5, and 4 hours after test material administration. The animals will be observed daily thereafter for at least 14 days for clinical signs and twice daily (morning and afternoon) for mortality. The duration of observations may be extended when considered necessary. The time of death will be recorded as precisely as possible.

Individual body weights will be recorded just prior to study initiation and at 7 and 14 days following test material administration and at death. Changes in body weight will be calculated and recorded when survival exceeds 1 day.

Pathology

All test animals, whether dying during the study or sacrificed at termination, will be subjected to a gross necropsy examination and abnormalities recorded.

Report

The final report will contain a description of the test material, a description of how the study was conducted, response data for clinical signs, mortality and body weights by sex, a discussion of the data, and gross pathology findings.

Maintenance of Raw Data and Records

Original data or copies thereof will be available at HLA to facilitate auditing the study during its progress and prior to acceptance of the final report. When the final report is completed, all original paper data, as well as the final report, will be retained in the archives of HLA, Madison, Wisconsin (OP-GEN 44).

REFERENCES

1. Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 401, Acute Oral Toxicity, adopted May 21, 1981.

2. 21 CFR 58.

3. DHEW Publications No. (NIH) 78-23 (1978).

PROTOCOL APPROVAL

Dallas D. Zimmerman, PhD
Sponsor's Representative
3M

Date

Steven M. Glaza
Study Director
Group Leader, Acute Toxicology
Hazleton Laboratories America, Inc.

2-25-85
Date

(1064S/jg)

HAZLETON LABORATORIES AMERICA, INC.
3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WI 53707 • (608) 241-4471 • TLX 703956 HAZRAL MDS UD

PROTOCOL TP2072

Primary Eye Irritation Study in Rabbits (OECD Guidelines)

Study No. 50202473

for

3M
St. Paul, Minnesota

by

Hazleton Laboratories America, Inc.
Life Sciences Division
3301 Kinsman Boulevard
Madison, Wisconsin 53704

February 25, 1985

PROTOCOL TP2072

Primary Eye Irritation Study in Rabbits
(OECD Guidelines)

Study No.	50202473
Study Location	Hazleton Laboratories America, Inc. Life Sciences Division 3301 Kinsman Boulevard Madison, Wisconsin 53704
Test Material	T-3727
Sponsor's Representative	Dallas D. Zimmerman, PhD
Study Director	Steven M. Glaza
Proposed Timetable	
Starting Date	Week of February 25, 1985
Completion Date	Week of March 1, 1985
Final Report Date	Week of April 1, 1985

OBJECTIVE

The objective of this study is to determine the level of irritation produced following a single exposure of a test material to one eye of albino rabbits. All aspects of this study will conform to the Organisation for Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 405, Acute Eye Irritation/Corrosion, Adopted May 12, 1981[1] and the U.S. Food and Drug Administration's Good Laboratory Practice Regulations for Nonclinical Laboratory Studies.[2] All procedures will be done according to Hazleton Laboratories America, Inc. (HLA) Standard Operating Procedures (SOPs) referenced in this protocol.

TEST MATERIAL

Identification

Test Material:	T-3727.
Physical Description:	Off-white solid.
Purity and Stability:	Sponsor has purity and stability determinations on file.
Storage Conditions:	Store at room temperature.
Test Material Retention:	Any unused test material will be discarded 30 days after issuance of final report.
Safety Precautions:	Laboratory personnel will take the normal necessary precautions in handling a substance of unknown toxicity. Laboratory clothing, latex gloves, safety glasses, and a particle mask approved for toxic dusts must be worn.

TEST SYSTEM

Test Animal

Young adult albino rabbits of either sex of the New Zealand White strain, approximately 14 weeks of age, will be obtained from Hazleton Research Products, Inc., Denver, Pennsylvania. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. The New Zealand White albino rabbit is the animal of choice based upon its large orbit and nonpigmented iris.

Acclimation

Upon receipt, the animals will be taken to a designated animal room where they will be acclimated for at least 1 week before being placed on test (OP-GENB 36). During acclimation, the animals will be examined for clinical abnormalities indicative of health problems (e.g., diarrhea, ectoparasites, rough hair coat, nasal or ocular discharge, evidence of injury, etc.). Any animals regarded as unsuitable for the study purposes because of poor physical condition will not be released from acclimation and the reason(s) will be documented.

Identification

Each animal in the study will be assigned a permanent identification number and will be identified with a metal ear tag (OP-GENB 24). All data collected from an animal will be recorded and filed under its identification number.

Housing and Maintenance

The following environmental conditions will be maintained in the animal room used for this study (OP-TARC 230).

- Temperature: 21°C ±2°
- Relative humidity: 50% ±20%
- Air change: At least 10 changes an hour of filtered 100% outside air
- Light cycle: 12 hours light/12 hours dark

Temperature and humidity will be monitored throughout the study. Variations from prescribed environmental conditions will be documented.

Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals."[3] Care will be taken to ensure that the animals are not disturbed for reasons other than data collection and routine maintenance. The animals will be housed individually in screen-bottom stainless steel cages (heavy gauge) held on racks, with absorbent pan liners in the urine- and feces-collecting pans. Pan liners will be changed at least three times each week.

Feed and water will be provided ad libitum. The diet will be Teklad Laboratory Rabbit Diet. No contaminants are expected to be present in the feed or water which would interfere and affect the results of the study.

Study Design

Three rabbits will be selected at random based upon health and a body weight of 2.0 to 3.5 kg.

PROCEDURES

Preparation and Administration of Test Material

The rabbits' eyes will be examined using fluorescein dye procedures within 24 hours prior to test material administration. Only animals with no sign of

corneal injury or eye abnormalities will be utilized. One eye of each animal will be treated with the test material and the other eye will serve as the untreated control.

Each rabbit will receive 0.1 g (or the weight equivalent of 0.1 mL) of solid test material. If necessary, the solid test materials will be finely ground into a dust or powder. The test material will be placed into the everted lower lid of the rabbit's eye. The upper and lower lids are then to be gently held together for 1 second before releasing to prevent loss of material. The eyes of the rabbits will remain unflushed for 24 hours following instillation of the test material. After 24 hours, a washout may be used if considered appropriate.

Reason for Route of Administration

Historically, the route of choice based on the method of Draize.[4]

Observations

The treated eyes of all animals will be examined for ocular irritation at 1, 24, 48, and 72 hours after treatment. If no irritation or injury is present at 72 hours, the study will be terminated. If irritation is present at 72 hours, additional observations will be made at 96 hours and at 7, 14, and 21 days. If at any of these time points there is no irritation, the study will be terminated. If injury is still present at 21 days, the Sponsor will be contacted to determine whether the study should continue or be terminated. After recording the 24-hour observations, sodium fluorescein may be used to aid in revealing possible corneal injury. Irritation will be graded and scored using the Draize technique (Attachment 1).[4] All eye abnormalities will be recorded.

All animals that have a damaged eye producing undue stress or discomfort will be sacrificed for humane reasons after consulting with the Sponsor.

Body weights will be recorded prior to test material administration and at weekly intervals throughout the study. Observations and body weights will be recorded in the study notebook.

Pathology

All animals, whether dying or sacrificed at study termination, will be discarded.

Report

The final report will present a description of the test material, a description of the test system, dates of study initiation and termination, a summary table showing the irritation data at each observation period, and any special observations that were recorded.

Maintenance of Raw Data and Records

Original data or copies thereof will be available at HLA to facilitate auditing the study during its progress and prior to acceptance of the final report. When the final report is completed, all original paper data, as well as the final report, will be retained in the archives of HLA, Madison, Wisconsin (OP-GEN 44).

REFERENCES

1. "Acute Eye Irritation/Corrosion," OECD Guidelines for Testing Chemicals, Section 405 (May 12, 1981).

2. 21 CFR 58.

3. DHEW Publications No. (NIH) 78-23 (1978).

4. Draize, J. H., Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics - Dermal Toxicity, Association of Food and Drug Officials of the U.S., Topeka, Kansas, pp. 49-51 (1959).

PROTOCOL APPROVAL

Dallas D. Zimmerman, PhD
Sponsor's Representative
3M

2-25-85
Date

Steven M. Glaza
Study Director
Group Leader, Acute Toxicology
Hazleton Laboratories America, Inc.

2-25-85
Date

(1068S/jg)

PROTOCOL - ATTACHMENT 1

(1) Cornea

(A) Opacity - degree of density (area most dense taken for reading)

No opacity	0
Scattered or diffuse area, details of iris clearly visible	1
Easily discernible translucent areas, details of iris slightly obscured	2
Opalescent areas, no details of iris visible, size of pupil barely discernible	3
Opaque, iris invisible	4

(B) Area of cornea involved

One quarter (or less), but not zero	1
Greater than one quarter, but less than half	2
Greater than half, but less than three quarters	3
Greater than three quarters, up to whole area	4

A x B x 5 Total Maximum = 80

(2) Iris

(A) Values

Normal	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive)	1
No reaction to light, hemorrhage, gross destruction (any or all of these)	2

A x 5 Total Maximum = 10

(3) Conjunctivae

(A) Redness (refers to palpebral conjunctivae only)

Vessels normal	0
Vessels definitely injected above normal	1
More diffuse, deeper crimson red, individual vessels not easily discernible	2
Diffuse beefy red	3

(B) Chemosis

No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of lids	2
Swelling with lids about half closed	3
Swelling with lids about half closed to completely closed	4

(C) Discharge

No discharge	0
Any amount different from normal (does not include small amounts observed in inner canthus of normal animals)	1
Discharge with moistening of the lids and hairs just adjacent to lids	2
Discharge with moistening of the lids and hairs, and considerable area around the eye	3

Score (A + B + C) x 2 Total Maximum = 20

The total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctivae.